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THE SOLVOLYSIS OF VARIOUS *p*-METHOXYNEOPHYL
ARYLSULFINATES

BY

JOHN MICHAEL NOREYKO

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE
OF MASTER OF SCIENCE

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FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled, "The Solvolysis of Various p-Methoxyneophyl Arylsulfates", submitted by John Michael Noreyko, B.Sc., in partial fulfilment of the requirements for the degree of Master of Science.

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- ABSTRACT -

The solvolysis of various *p*-methoxyneophyl arylsulfonates has been examined in 80% and 100% by vol. ethanol, using sodium ethoxide, potassium acetate, and 2,6-lutidine as bases. The aryl groups included phenyl, 2-tolyl, 4-tolyl, 2-chlorophenyl, and 2,6-dimethylphenyl. The rates were followed by infrared spectrophotometric techniques.

Examination of kinetic data and product analyses disclosed that all esters underwent exclusive sulfur-oxygen bond cleavage with no carbon-oxygen bond cleavage discernible.

Sulfur-oxygen bond cleavage was found to be extremely slow when 2,6-lutidine was used as base, even when the reaction was carried out in 60% ethanol, at 90°C. Under the same conditions, the solvolysis proceeded about 2000 times faster when acetate ion was used as base. Good pseudo-first-order kinetics were obtained for every compound and a linear dependence of rate on acetate concentration was also established.

The order $\text{EtO}^- > \text{OAc}^- > \text{N}_3^- > \text{SCN}^- > 2,6\text{-lutidine}$ expresses the relative effectiveness of these nucleophiles found for promoting sulfur-oxygen bond cleavage.

The effect of variation of substituents in the sulfonate group on sulfur-oxygen bond cleavage is discussed and the data are compared with similar experiments carried out in the study of $\text{B}_{\text{ac}2}$ hydrolysis of alkyl benzoates, by other authors.

The reaction was found to exhibit a definite solvent effect when the polarity of the medium was varied from 100% to 60% ethanol.

The results are consistent with rate-determining nucleophilic displacement on sulfur by such bases as acetate ion,

to form the unstable mixed anhydride, which undergoes rapid decomposition to give products.

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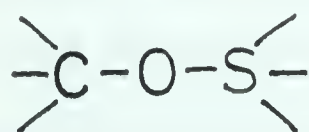
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INTRODUCTION

The base catalysed cleavage of sulfur-oxygen bonds in compounds of the general structure I has been investigated by many authors. The cases which are of particular interest are those in which there is the possibility of attack on either sulfur or carbon by the nucleophilic species to give rise to



I



II

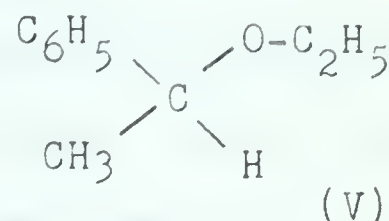
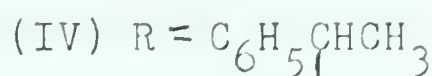
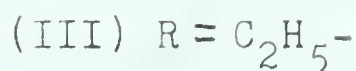
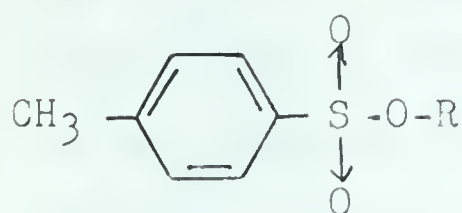
sulfur-oxygen or carbon-oxygen bond cleavage respectively. The extent of this competition for the nucleophile may be illustrated by considering the behavior of certain classes of these compounds drawn from the literature.

The hydrolytic stabilities of alkyl sulfenates (II) appear to be somewhat greater than those of the corresponding aryl derivatives.¹ Zincke^{1a} found that, if the phenyl sulfenates were not kept in a vacuum desiccator, rapid decomposition, with the formation of phenol, occurred. If R is 2,4-(NO₂)₂C₆H₃⁻, however, Kharasch^{2,2a} has pointed out that these compounds can be used to characterize aliphatic alcohols since quite stable, crystalline esters are formed on treatment of the alcohol with the corresponding sulfenyl chloride.

The mechanism of decomposition of these esters in an ionizing medium has not, as yet, been examined intensively. Therefore, a comparison of the extent of sulfur-oxygen or carbon-oxygen bond cleavage cannot be properly made in this case.

The esters of sulfonic acids have long been known for their alkylating properties. For example, if ethyl p-toluenesulfonate

III is treated with ethoxide ion in ethanol, a good yield of diethyl ether is obtained by a process which exhibits good second-

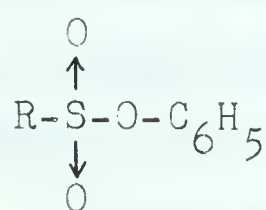


order kinetics ^{3,4}. Kenyon, Phillips and Taylor⁵ observed that l-phenylmethylcarbinyll p-toluenesulfonate (IV) was converted to the inverted d-ether (V) on refluxing the compound in absolute ethanol containing some potassium carbonate. Additional work by Kenyon, Phillips and Pittman⁶ pointed out that treatment of d-2-butyl, d-2-octyl, and d-benzylmethylcarbinyll p-toluenesulfonates with potassium thiocyanate in refluxing ethanol gave the corresponding thiocyanates with inversion of configuration. This evidence shows clearly that, in these systems, carbon-oxygen bond cleavage is the faster reaction, going, in fact, to completion without any appreciable attack on sulfur by the nucleophilic species.

More recently, similar results were obtained by Colter and Johnson⁷ who treated various p-substituted 2-pentyl benzenesulfonates with sodium ethoxide in absolute ethanol. They obtained the usual E_2 products but could not observe any evidence for concurrent sulfur-oxygen bond cleavage.

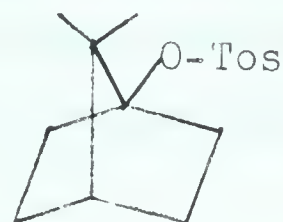
The phenyl esters of sulfonic acids seem to be exceptions to the rule. Otto⁸ first observed that the hydrolysis of phenyl p-toluenesulfonate, in dilute aqueous alkali, proceeded much slower than what was observed for the corresponding alkyl derivatives. More recently, Bunton and co-workers^{9,10} have found that the alkaline hydrolysis of phenyl p-toluenesulfonate (VI) and phenyl

methanesulfonate (VII) in aqueous dioxane enriched with H_2O^{18} at 100°C . afforded phenol containing no labelling in either case. In addition, there was little difference between the rates of hydrolysis of the two systems. If the hydrolysis was attempted in the absence of hydroxide ion, no reaction ensued. From these details, Bunton concluded that sulfur-oxygen bond cleavage constituted approximately 98% of reaction.



(VI) $\text{R} = \text{p-CH}_3\text{C}_6\text{H}_4-$

(VII) $\text{R} = \text{CH}_3-$



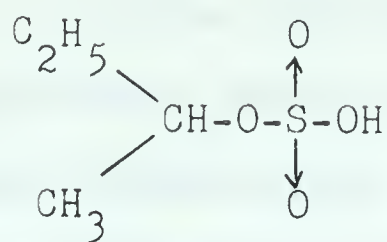
(VIII)

Bartlett and Knox¹¹ found another exception in the solvolysis of 7,7-dimethylbicyclo(2,2,1)heptan-1-yl p-toluenesulfonate (VIII). This compound proved to be inert to the highly nucleophilic reagent, lithium iodide in boiling acetone.

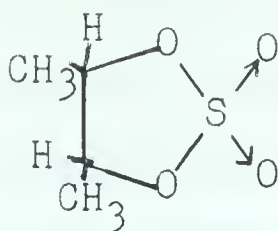
The lack of reactivity of these compounds toward carbon-oxygen bond cleavage may be explained by the virtual impossibility of back-side attack by the nucleophilic species on the tertiary carbon. Ionization of the carbon-oxygen bond is also excluded since the requirement of coplanarity cannot be possessed by either incipient ion.

The esters of sulfuric acid are quite analogous to sulfonates in their behavior. Nef¹² found that treatment of ethyl sulfate with alcoholic potassium hydroxide solution gave a 50% yield of diethyl ether. Similarly, (+)-2-butyl hydrogen sulfate (IX) hydrolysed in aqueous alkali to give 54% (-)-2-butanol of inverted configuration, and 8% butylene¹³.

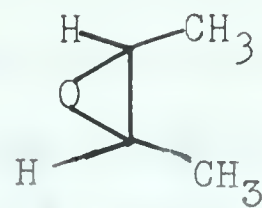
Likewise, Garner and Lucas¹⁴ hydrolysed d-(-)-trans-1,2-dimethylethylene sulfate (X) in aqueous 2N potassium hydroxide



(IX)



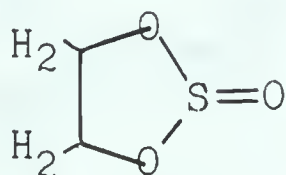
(X)



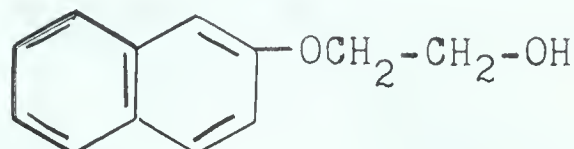
(XI)

solution to obtain mainly dl-glycol with 15% meso and 2% d-glycol. The formation of racemic product under basic conditions may be accounted for by postulating the formation of the cis-oxide intermediate (XI), which, on hydration, would result in the dl-glycol.

Organic sulfites would seem to bear a closer resemblance to the system to be studied. If an excess of ethylene sulfite (XII) is treated with β -naphthol in dilute methanolic sodium hydroxide solution, an appreciable yield of the β -naphthyl ether (XIII) is obtained¹⁵. This result could be explained by

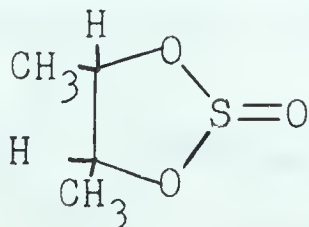


(XII)

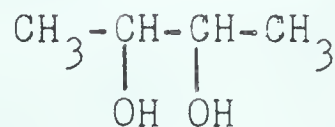


(XIII)

a nucleophilic attack by β -naphthoxide ion on carbon to give carbon-oxygen bond cleavage. The bulky nature of the attacking species would presumably prevent attack on sulfur. Garner and Lucas¹⁴ treated a similar compound, d-(-)-trans-1,2-dimethylethylene sulfite (XIV), with aqueous 2N potassium hydroxide solution but obtained the diol (XV) of retained configuration. Here, sulfur-oxygen bond cleavage occurred at a much faster rate than the corresponding attack on carbon to give racemization.

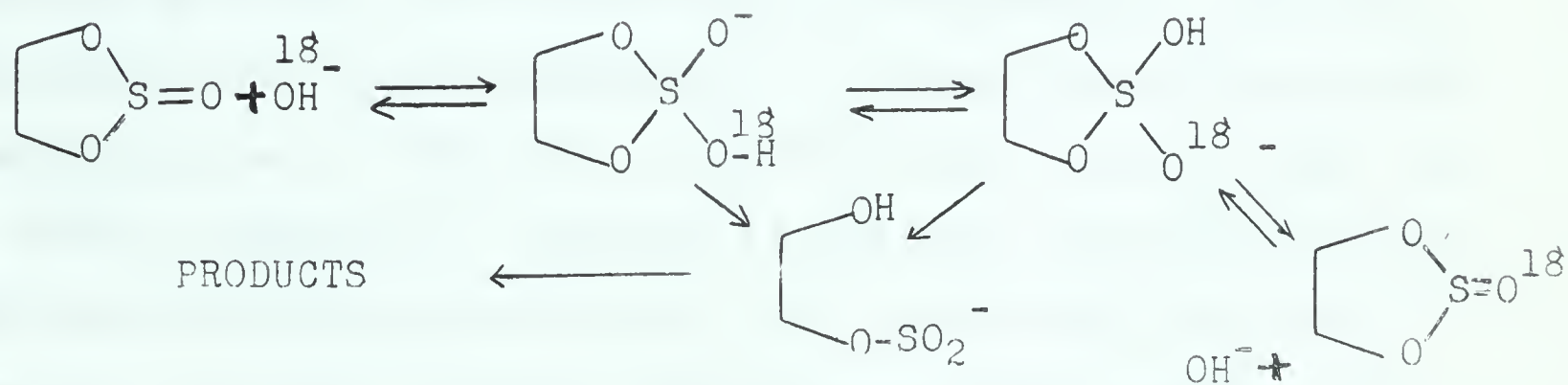


(XIV)

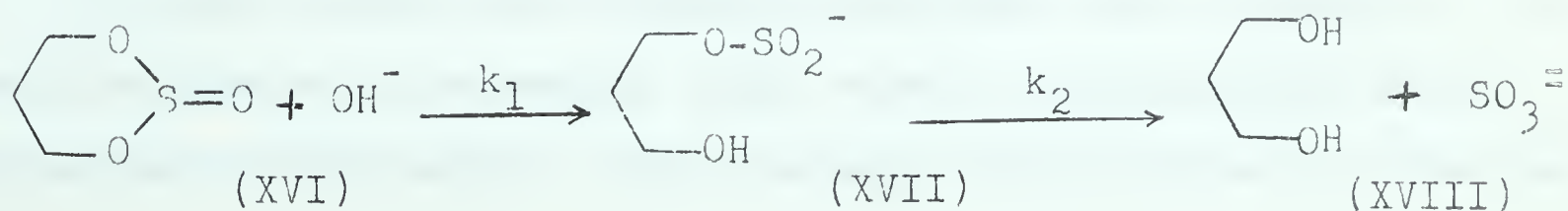


(XV)

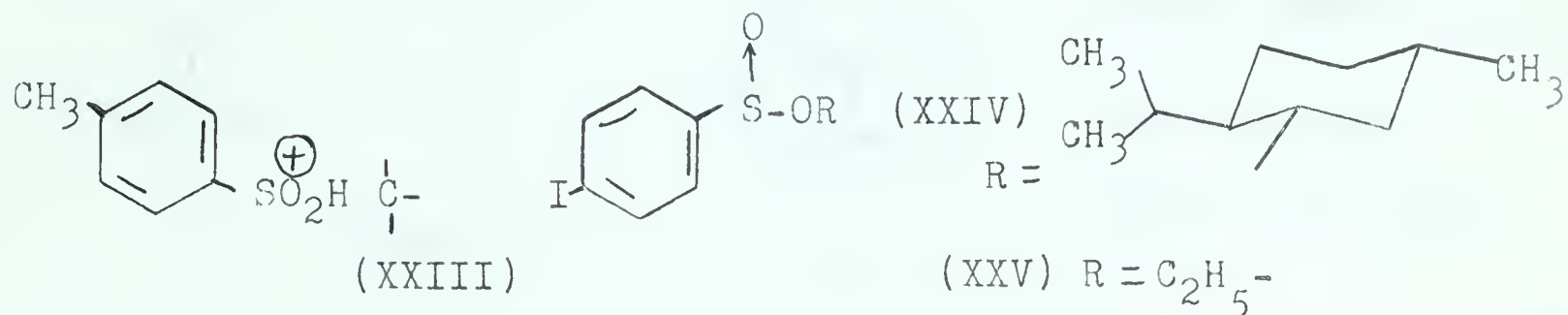
In the hydrolysis of 1,2 and 1,3 cyclic sulfites under basic conditions, Bunton, de la Mare, Tillett and co-workers¹⁶ had found that sulfur-oxygen bond cleavage was the only observable reaction. After hydrolysis of ethylene sulfite in H_2O^{18} enriched dilute aqueous alkali, the authors found that the glycol product had incorporated no O^{18} into the molecule. However, sulfite recovered after partial hydrolysis in this medium was found to contain 0.016 atom % excess of sulfinyl O^{18} as compared with 0.940 % excess for H_2O (solvent). Bunton interpreted this result to mean that the exchange reaction did not occur in significant competition with the actual hydrolysis. Davis¹⁷, in a recent paper, suggested that the small amount of exchanged material could have arisen from an intermediate similar to that proposed for $B_{ac}2$ ester hydrolysis¹⁸.



Bunton also examined the alkaline hydrolysis of trimethylene sulfite (XVI)¹⁹. It was found to exhibit second-order kinetics, first-order in both base and sulfite respectively. The fact that the rate was the same if either the rate of sulfur dioxide production or the rate of consumption of base was measured, together with the data collected on the other systems, led the author to propose the following scheme of hydrolysis:



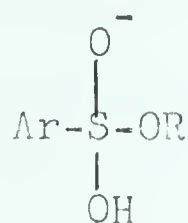
configuration was recovered. In the absence of carbonate, catalysis by the developing acid would presumably occur, thus facilitating displacement on carbon due to the formation of the better leaving group (XXIII). The final result in this case would be inversion plus racemization.



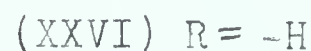
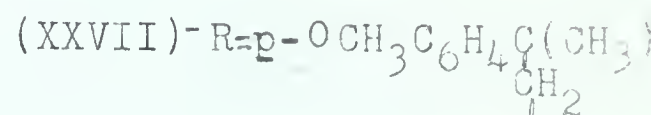
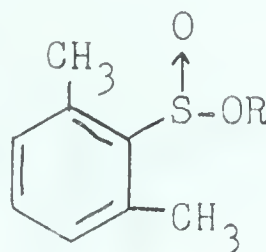
More recently, Herbrandson and Cusano²² studied the solvolysis of (-)-menthyl (+)-p-iodobenzenesulfinate (XXIV) in absolute ethanol with sodium ethoxide as base. The sole product of the reaction was the corresponding ethyl ester (XXV). The optical activity of the reaction mixture at the completion of the ethanolysis corresponded to that value to be expected from a concentration of (-)-menthol, equivalent to the amount of ester originally present. This, together with the fact that the pseudo-first-order reaction was truly second-order, i.e., first-order in both ester and base respectively, would seem to be good evidence for the attack by ethoxide ion on sulfur in the rate determining step. Again, no evidence for carbon-oxygen bond cleavage was obtained.

These results are in fine agreement with recent work by Bunton and Hendy^{23,24} on the hydrolysis of methyl and benzhydryl p-toluenesulfonates in H_2O^{18} enriched, 60% by vol. dioxane-water, using sodium hydroxide as base. These authors found that at 0°C ., extremely rapid second-order displacement by hydroxide ion occurred ($k_2 \approx 0.05$ and 0.11 l/mole sec. res-

pectively), to give exclusive sulfur-oxygen bond cleavage with no O^{18} incorporation into the alcoholic product. No sign of alkyl-oxygen bond fission was observed, but no evidence for the formation of an intermediate having the general form (XXVa) was obtained.

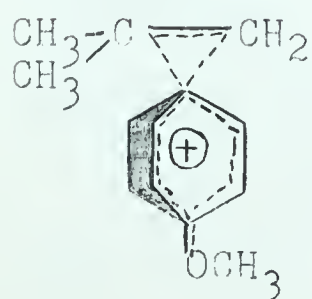


(XXVa)

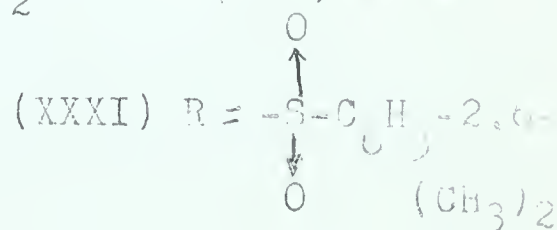
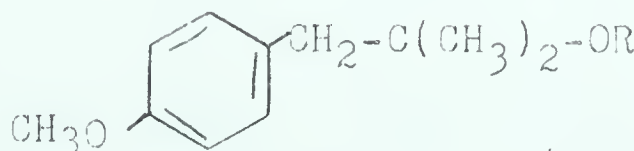


From the above dissertation, it would appear that, under the appropriate conditions, either sulfur-oxygen or carbon-oxygen bond cleavage can take place. In order to obtain more information about the extent of these processes in such systems, the following project was undertaken. Initially, a system was required in which one could conveniently distinguish between the two bond fissions.

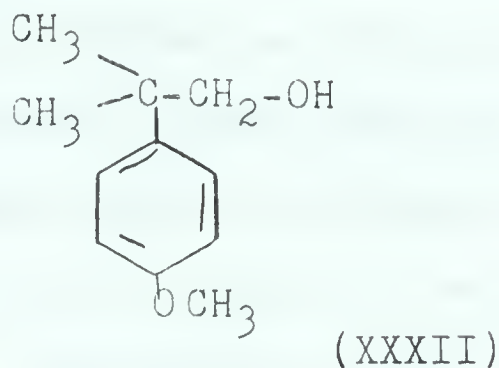
This was accomplished by the choice of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) as the initial ester for study. The reason for this choice lay in the fact that if carbon-oxygen bond fission occurred, the ester would give rise to the long lived, non-classical ion (XXVIII)²⁵, which could partition itself among the various solvolysis products, such as rearranged ether (XXIX), or alcohol (XXX), or perhaps recombine with the sulfinate ion to give sulfone (XXXI).



(XXVIII)



If, on the other hand, sulfur-oxygen bond cleavage took place, it could be easily detected by the presence of p-methoxyneophyl alcohol (XXXII). If the reaction was carried out in absolute ethanol, the corresponding ethyl ester (XXXIII) would be a possible product.



PART I

INITIAL EXPLORATORY TITRIMETRIC RATES

RESULTS

The preparation of p-methoxyneophyl alcohol (XXXII) was carried out according to the method of Winstein and Heck²⁵. This involved the cyanation of anisyl chloride, obtained from anisyl alcohol, with sodium cyanide, followed by dimethylation of the resulting nitrile with an excess of methyl iodide, in the presence of sodium amide. Hydrolysis of the dimethylated cyanide with 50% aqueous methanolic potassium hydroxide, followed by lithium aluminum hydride reduction of the acid product afforded p-methoxyneophyl alcohol (XXXII).

Diazotization of 2,6-dimethylaniline, followed by treatment of the diazonium salt with sulfur dioxide in the presence of finely divided copper, gave 2,6-dimethylbenzenesulfinic acid (XXVI). Reaction of the corresponding acid chloride, obtained from acid (XXVI) by treatment with thionyl chloride, with alcohol (XXXII) in pyridine, at dry-ice temperatures, afforded p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII).

The use of ethoxide as base

It was initially decided to follow the rate of solvolysis of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) titrimetrically, using sodium ethoxide as base, in 80% by volume ethanol-water mixtures. A few rates were carried out at 90°C. using the sealed tube method (see experimental p. 86) and the results are given in Table I.

All the runs tabulated showed a large inconsistent drift in rate as reaction proceeded. This may be clearly seen upon exam-

- Table I -

THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE
(XXVII) IN 80% by vol. ETHANOL AT 90°C. WITH SODIUM ETHOXIDE AS
BASE.

Run	[Ester] M	[EtO ⁻] M	% Base Consumed ^a	in T hrs.	Lab Book ^b Ref.
1	0.02538	0.02966	113	25	66-1
3	0.02494	0.02434	98.2	25	70-1
5	0.02573	0.03327	112.2	25	72-1
6	0.02556	0.03603	132.5	25	74-1
14	0.01868	0.03240	155.3	20	80-1
17 ^c	0.02464	0.01822	67.4	25	91-1
18 ^c	0.02508	0.03280	97.4	60	92-1
21 ^c	0.02553	0.02274	59.8	48	99-1

a- Base consumed based on 100% total acid produced if all ester gives acid.

b- Refers to the location of the rate in the laboratory note book. The first number refers to the page number, the second, to the book number.

c- These rates were carried out at 50°C.

ination of a sample rate (Table II), and a plot of the data contained therein (Fig.1). Curiously, in every case where the base concentration exceeded the ester concentration, an abnormally large consumption of base had occurred. The drift in rate would tend to suggest the existence of a process of higher order, perhaps the reaction of two different compounds.

This drift could possibly be ascribed to some impurity present in the system, which was solvolysing at a very great speed. To check this hypothesis, ester (XXVII) and materials from which it was prepared were examined with respect to their purity.

The p-toluenesulfonate ester of p-methoxyneophyl alcohol (XXXII), was prepared and its acetolysis was carried out at 50°C. A first-order rate of acid production was obtained ($k_1 = 1.18 \pm 0.06 \times 10^{-4} \text{ sec.}^{-1}$) which compared quite favorably with the value obtained by Winstein and Heck ($1.21 \pm 0.02 \times 10^{-4} \text{ sec.}^{-1}$).²⁵ Consequently, the impurity did not come from p-methoxyneophyl alcohol (XXXII).

2,6-Dimethylbenzenesulfinic acid (XXVI) was also examined to see if it was stable under the reaction conditions. Pure material, recrystallized from ethyl acetate (m.p. 94.6 - 96.0°C.), was found to be 97 - 99% pure on titration of a sample with standard sodium hydroxide solution. Samples of this substance were subjected to the reaction conditions for an extended period of time (Table III).

The recovery of 80% starting material in run 25, together with the abnormally high consumption of base which had occurred, suggested that the base itself was decomposing under these conditions.

-Figure 1-

Run # 6: The solvolysis of p-methoxyneophyl
2,6-dimethylbenzenesulfinate (XXVII) in 80%
by vol. ethanol-water, with sodium ethoxide
as base, at 90°C. Plot of disappearance of
base with time.

$$[\text{Ester}] = 0.02556\text{M}$$

$$[\text{Base}] = 0.03603\text{M}$$

Log(a-x)

0.5
0.4
0.3
0.2
0.1
0.0
1.95

$t \times 10^{-2}$ sec.

50

0

- Table II -

RUN# 6 ON p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) IN 80% by vol. ETHANOL-

WATER WITH SODIUM ETHOXIDE AS BASE AT 90°C.

[Ester]=0.02556M ; [Base]=0.03603M

Time	ml. Acid	x	(a-x)	Log(a-x)	$\frac{\text{Log}(a-x_1)}{(a-x_1)}$	$\frac{2.303}{t}$	$k_1 \times 10^3$	$\frac{-1}{\text{sec.}}$
t_0	4.012	-	-	-	-	-	-	-
t_{0t}	3.675	-	3.446	0.5370	After two minutes equilibration in the const. temp. bath.			
2 min.	3.023	0.652	2.794	0.4450	0.0910	0.01915	1.74	
4 min.	2.773	0.902	2.544	0.4040	0.1310	0.0096	1.26	
6 min.	2.664	1.011	2.435	0.3862	0.1505	0.0064	0.963	
8 min.	2.595	1.080	2.366	0.3735	0.1620	0.0048	0.778	
13 min.	2.494	1.181	2.265	0.3544	0.1817	0.00296	0.538	
18 min.	2.416	1.259	2.187	0.3390	0.1964	0.00214	0.421	
28 min.	2.273	1.402	2.044	0.3092	0.2258	0.0014	0.302	
58 min.	1.805	1.870	1.576	0.1965	0.3390	0.00066	0.224	
1 hr.								
58 min.	1.155	2.520	0.926	1.9660	0.5700	0.00033	0.188	

$$k_1 = \frac{2.303}{t} \text{Log} \frac{(a-x_1)}{(a-x_t)}$$

where $a = t_0 - t_\infty$ and $a = 3.783$ ml. acid

[Acid]=HClO₄ in dioxane = 0.04496M

If 100% reaction of ester occurs, 2.845 ml. acid is equivalent to the base consumed.

Therefore, % reaction occurring here is (a/2.845) x 100=132.5%.

This possibility was investigated by running control runs on solutions of ethoxide in 80% ethanol at 90°C. The results in Table IV verify this assumption.

Corrosion of the inside of the ampoule by hot alkali would seem to be the best explanation of the data obtained since the determination made under an atmosphere of nitrogen would exclude, at least as a major factor, oxidation of the alcohol by air. Similar results have been obtained by Westheimer and Metcalf²⁶ who found that at 55°C., the molarity of a 0.03 M solution of sodium ethoxide in 70% ethanol (by vol.) changed about 0.4% per hour. This value would correspond to roughly 82% base consumption after 240 hours; a value quite comparable with runs 28 & 29.

The fate of sulfinate ester (XXVII) under these conditions was next examined. Two product runs were allowed to proceed for 25 - 43 hours under the reaction conditions given above. The reaction mixture was neutralized with dilute acid, ether extracted and the ether layer was washed with 10% sodium carbonate solution. After the ether extract had been dried over anhydrous magnesium sulfate, the solvent was removed in vacuo and the residue separated into its components by elution chromatography. The fact that alcohol (XXXIII), and not rearranged alcohol (XXX), was obtained (Table V) would tend to indicate that only sulfur-oxygen bond cleavage products had been obtained and that little or no attack on carbon had occurred.

The use of weaker bases

Since the solvolysis with ethoxide as base proceeded at such a fast rate, it was decided to try weaker bases in its place to see if a more amenable situation could be obtained.

The compounds chosen as bases were sodium acetate and 2,6-

- TABLE III -

SUMMARY OF BLANK RUNS ON 2,6-DIMETHYLBENZENESULFINIC ACID (XXVI)

IN 80% by vol. ETHANOL-WATER WITH SODIUM ETHOXIDE AS BASE AT 90°C.

<u>Run</u>	<u>[Acid] M</u>	<u>[EtO⁻] M</u>	<u>% Base Consumed^a</u>	<u>in T hrs.</u>	<u>Lab Book Ref.</u>
22	0.01905	0.04949	125	85	104-1
25 ^b	0.01982	2.602	350	168	112-1

a- By base consumed is meant the amount of base consumed in excess of that required to neutralize the acid present.

b- In run 25, 80% of acid (XXVI) was isolated from the reaction mixture upon acidification and ether extraction of the resultant solution.

- TABLE IV -

SUMMARY OF BLANK RUNS CARRIED OUT ON SODIUM ETHOXIDE IN 80% by vol.

ETHANOL-WATER AT 90°C.

<u>Run</u>	<u>Initial [EtO⁻] M</u>	<u>% Base Consumed</u>	<u>in T hrs.</u>	<u>Lab. Book Ref.</u>
27	0.2851	85	362	116-1
28	0.03505	90.5	547	117-1
29 ^a	0.02558	85	166	117-1

a- Here, the run was carried out under an atmosphere of nitrogen.

- TABLE V -

SUMMARY OF PRODUCT RUNS CARRIED OUT ON p-METHOXYNEOPHYL 2,6-DI-METHYLBENZENESULFINATE (XXVII)^a IN 80% by vol. ETHANOL-WATER AT 90°C. WITH SODIUM ETHOXIDE AS BASE.

Run	[Ester]M	[EtO ⁻]M	% Base ^c Consumed in T hrs.	Products	% Yield	Lab. Book Ref.	
36	0.02583	0.04630	164	43	Alcohol (XXXII)	85	141-1
					Acid (XXVI)	73	
37	0.02782	0.04065	142	25	Alcohol (XXXII)	68	149-1
					Acid (XXVI)	21	
					Ester (XXVII)	18] - b
					Ester (XXXIII)	9	

a- The ester (XXVII) used had been purified by chromatography (elution) before use.

b- Estimated values from an infrared spectrum of a mixture of the two esters obtained in one chromatography fraction.

c- Base consumed (%) based on total acid produced from ester = 100%.

lutidine. Sodium acetate had the advantage of forming a buffered medium such that the acid produced in the solvolysis would not affect the pH of the medium to any great extent, thus preventing any acid catalysis. Its chief disadvantage lay in its sparing solubility in absolute ethanol. This problem was later solved by the use of the more soluble potassium salt.

The poor nucleophilicity of 2,6-lutidine, which may be ascribed to the steric effect of the two methyl groups adjacent to the nitrogen, coupled with its solubility in both ethanol and water, made it an obvious alternate choice. Fortunately, a buffered solution of lutidinium ion and lutidine has approximately the same pH as the comparable sodium acetate-acetic acid system, and can be titrated for lutidinium ion using phenolphthalein as indicator.

A series of rates were carried out on p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) using these bases in various aqueous ethanolic solutions. The results are tabulated in Table VI. It is quite clear from this data that the rate of acid formation observed here is extremely slow in comparison with the rate of base consumption in those runs on this compound carried out in the presence of ethoxide. In addition to this, examination of the reaction mixture in run 11 resulted in 80% recovery of starting material, i.e., ester (XXVII), after 25 hours at 90°C. Confirmation of this fact is given in runs 15 & 16, in which, after a point had been titrated for developing acid (12% reaction in 70 hours), an excess of 0.03M sodium methoxide was added and the mixture heated for 9-12 hours on a steam bath. Consequent titration of the excess base evidenced 100% reaction of the ester. Examination of the reaction mixture, afforded

- TABLE VI -

SUMMARY OF RATES CARRIED OUT ON p-METHOXYNEOPHYL 2,6-DIMETHYL
BENZENESULFINATE (XXVII) AT 90°C. IN AQUEOUS ETHANOL.

Run	[Ester] M	[Base] ^a M	% Acid Produced	in T hrs.	Solvent ^b	Lab. Book Ref.
7 ^c	0.02624	0.0500	11.2	25	80% EtOH-H ₂ O	54-1
8 ^c	0.02516	0.0500	10.5	25	"	58-1
9 ^c	0.02523	0.0500	10.8	25	"	60-1
10	0.02457	0.0500	6.03	25	"	62-1
11	0.02574	0.0500	4.22	25	"	64-1
12	0.02401	0.0500	6.00	271	"	76-1
13	0.02522	0.0500	9.87	144	"	78-1
15	0.02503	0.0500	10.6	96	"	82-1
16	0.02502	0.0500	8.90	70	"	90-1
26	0.02518	0.05023	23.8	60 days	60% EtOH-H ₂ O	114-1
30	0.02562	0.04796	14.0	73 days	"	121-1
31	0.02708	0.05320	16.8	71 days	"	123-1
33 ^d	0.00866	0.01469	6.82	49 days	40% EtOH-H ₂ O	128-1

a- All rates were carried out using sodium acetate as base except for runs 30, 31, and 33 which utilized 2,6-lutidine as base.

b- All aqueous ethanol solutions are % by volume.

c- Runs carried out on crude ester, before chromatography.

d- Small concentration of ester due to its low solubility in the solvent.

only p-methoxyneophyl alcohol (XXXII) and 2,6-dimethylbenzenesulfonic acid (XXVI).

Analogous data was obtained for those rates using 2,6-lutidine as base. Again (Table VII), rate of solvolysis is found to be quite slow, in fact, slower than the case in which sodium acetate was used as base.

- TABLE VII -

SUMMARY OF PRODUCT RUNS CARRIED OUT ON p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) AT 90°C. WITH 2,6-LUTIDINE AS BASE.

Run	[Ester] M	[Base] M	Solvent ^a % EtOH	Rxn. Time	Products	% Recovery	Lab. Book Ref.
34	0.00449	0.02296	40	60 days	Ester (XXVII)	75	130-1
					Alcohol (XXXII)	25	
35	0.02539	0.04161	60	46 days	Ester (XXVII)	85	132-1
					Alcohol (XXXII)	6	

a- The solvent used in both runs was % by volume, ethanol-water.

PART I

DISCUSSION

No quantitative conclusions could be drawn from the titrimetric rates, regardless of the base used. However, the results clearly indicated that reaction proceeded very rapidly with ethoxide ion as base. Reaction rate was much slower with the less basic nucleophiles but could not be followed by titration. It therefore appeared necessary to investigate other analytical techniques to clarify these data.

PART II

SPECTROPHOTOMETRIC RATES

Initially, both ultraviolet and infrared spectrophotometric methods were investigated in order to determine if p-methoxy-neophyl 2,6-dimethylbenzenesulfinate (XXVII) possessed some characteristic peak whose disappearance could be measured with some accuracy. The ultraviolet region proved fruitless since ester (XXVII) and the known products of its solvolysis, ethyl 2,6-dimethylbenzenesulfinate(XXXIII), and p-methoxyneophyl alcohol (XXXII), had similar spectra.

The infrared region proved more successful. Ester (XXVII) was found to have a characteristic peak at 10.42 microns which was not masked by any peaks possessed by the known products or of the solvent, carbon disulfide. Similarly, ethyl ester (XXXIII) formation could be monitored from a sharp peak which it possessed at 11.35 microns.

It was first established that these absorptions for ester (XXVII) and ethyl ester (XXXIII), mentioned above, obeyed the Lambert-Beer law over the concentration ranges studied and that these materials could be reproducibly isolated from the reaction mixture to obtain this correlation (see experimental section).

-RESULTS-

A- Rates with ethoxide as base

Rates were subsequently carried out on ester (XXVII) in 80% by volume ethanol-water, with sodium ethoxide as base, at 25°C. The results of these experiments are given in Table VIII. A sample rate extracted from these data is presented in Table IX,

- TABLE VIII -

SUMMARY OF RUNS CARRIED OUT ON p-METHOXYNEOPHYL 2,6-DIMETHYL-
BENZENESULFINATE (XXVII) IN 80% by vol. ETHANOL-WATER AT 25°C.
WITH SODIUM ETHOXIDE AS BASE.

Run	$[\text{EtO}^-] \text{ M}$	$[\text{Ester}] \text{ M}$	$k_1^d \times 10^4 \text{ sec}^{-1}$	$k_1^a \times 10^4 \text{ sec}^{-1}$	$\frac{k_1^d}{[\text{EtO}^-]} \times 10^3 \text{ l/mole sec.}$	Lab. Book Ref.
39	0.05051	0.02450	3.02 ± 0.39	-----	5.94	185-1
40	0.04620	0.02433	3.08 ± 0.36	-----	6.68	187-1
44	0.05128	0.02445	3.00 ± 0.09	-----	5.87	145-2
53a	0.05124	0.02419	2.83 ± 0.06	2.48 ± 0.21	5.53	150-2
59	0.05024	0.02410	2.82 ± 0.09	2.21 ± 0.13	5.61	151-2
61	0.02806	0.02424	1.62 ± 0.07	1.57 ± 0.06	5.70	152-2
64	0.03603	0.02422	2.01 ± 0.06	2.03 ± 0.14	5.58	153-2
65	0.06470	0.02424	3.70 ± 0.09	3.62 ± 0.05	5.72	154-2
66	0.09729	0.02419	5.51 ± 0.23	6.38 ± 1.63	5.66	155-2
67	0.01368	0.02417	0.668 ± 0.056	0.703 ± 0.035	4.88	156-2

k_1^d = First-order rate of disappearance of ester (XXVII).

k_1^a = Initial first-order rate of appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII).

RUN # 61 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) IN 80% by vol. ETHANOL-WATER AT 25°C. with SODIUM ETHOXIDE AS BASE. $[\text{Ester}] = 0.02424\text{M}$; $[\text{EtO}^-] = 0.02806\text{M}$

$t_{\text{sec.}}$	ml. Acid	$\text{Log} \left[\frac{I_0}{I} \right]^d$	$\text{Log} (a-x)$	$\text{Log} \left[\frac{I_0}{I} \right]^a$	$\text{Log} (D_{\infty}-D)$	$\text{Log} \left(\frac{D_{\infty}-D_0}{(D_{\infty}-D)} \right)$	$\frac{2.303}{t} \times 10^4$	$k_1^d \frac{1}{\text{sec.}}$	$k_1^a \frac{1}{\text{sec.}}$
0	2.559	1.38928	0.14280	0.05124	0.10870	---	---	---	---
600	2.511	1.32991	0.12382	0.17609	0.05456	0.05414	38.4	0.728	2.07
1080	2.480	1.24716	0.09596	0.23726	0.03048	0.07822	21.3	1.00	1.66
1860	2.420	1.05331	0.02255	0.34727	1.98349	0.12521	12.4	1.49	1.55
2820	2.372	0.84737	1.92859	0.47173	1.92340	0.18530	8.16	1.74	1.51
3660	2.329	0.74317	1.87109	0.51175	1.90211	0.20659	6.28	1.71	1.30
4560	2.368	0.66763	1.82454	0.59025	1.85715	0.25155	5.05	1.60	1.26
6540	2.273	0.48231	1.68333	0.67155	1.80509	0.30362	3.52	1.63	1.07
8820	2.148	0.32411	1.51069	---	---	---	2.61	1.65	---
10620	2.076	0.25634	1.40882	---	---	---	2.17	1.59	---
14040	1.908	0.16726	1.22340	---	---	---	1.64	1.51	---

Acid HCl 0.05253M. $\text{Log} \left[\frac{I_0}{I} \right]^d = (a-x)$ k_1^d = Rate of disappearance of ester (XXVII).

$\text{Log} \left[\frac{I_0}{I} \right]^a = D$ k_1^a = Initial rate of appearance of ethyl ester (XXXIII).

$D_{\infty} = 1.3100$
 k_1^d (average) = $1.62 \pm 0.07 \times 10^{-4} \text{ sec.}^{-1}$
 k_1^a (average) = $1.57 \pm 0.06 \times 10^{-4} \text{ sec.}^{-1}$

In the calculation of k_1^a , a theoretical infinity D_{∞} was used. This value was derived from a Lambert-Beer plot for (XXXIII) and corresponds to the amount of (XXXIII) present at t_{∞} if no decomposition of this ester had occurred.

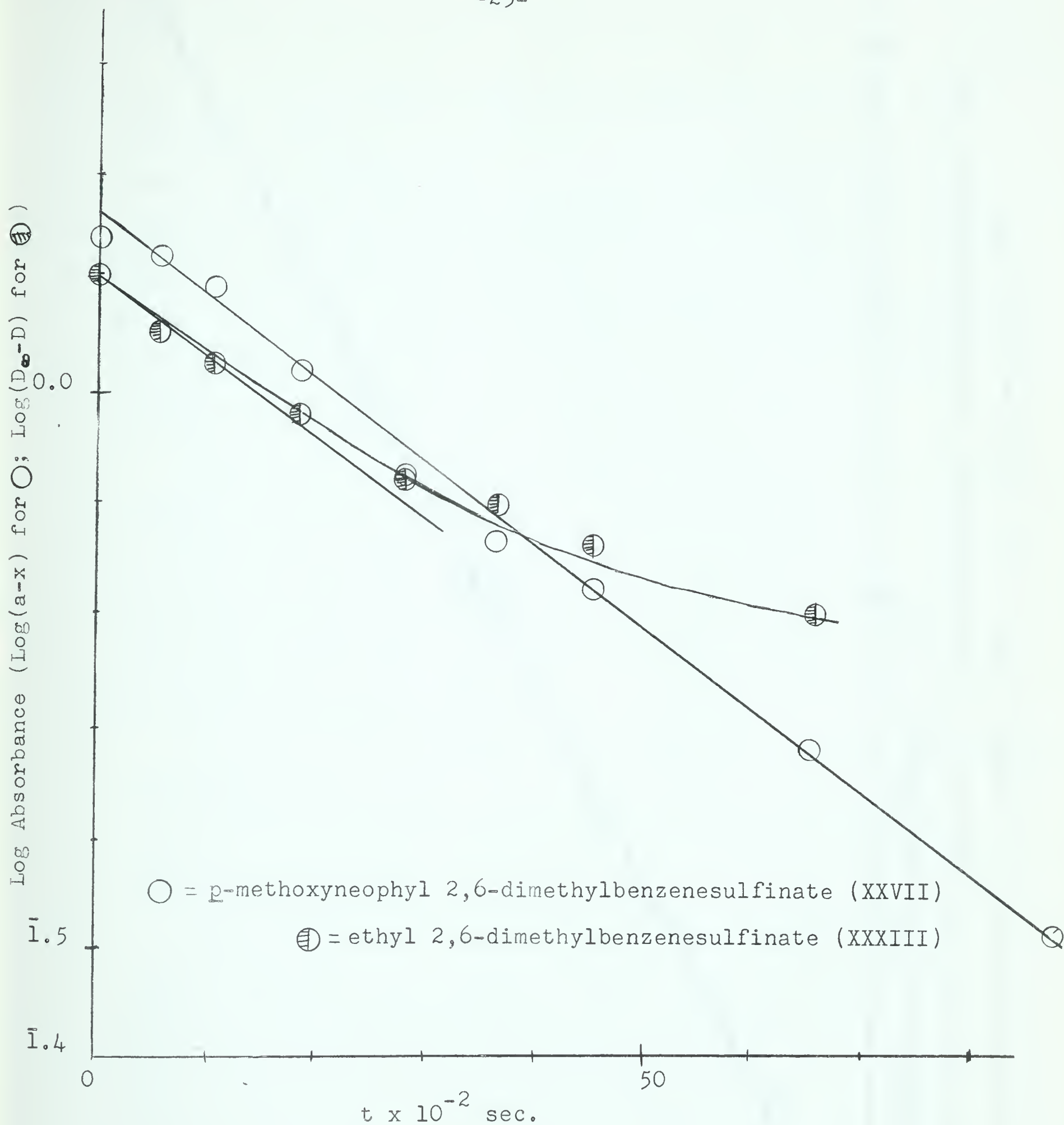


Figure 2: Plot of rate of disappearance of ester (XXVII), and rate of appearance of ethyl ester (XXXIII), in run 61, in 80% ethanol at 25°C, with sodium ethoxide as base. (see data in Table IX).

$$[\text{Ester XXVII}] = 0.02424\text{M}$$

$$[\text{NaOEt}] = 0.02806\text{M}$$

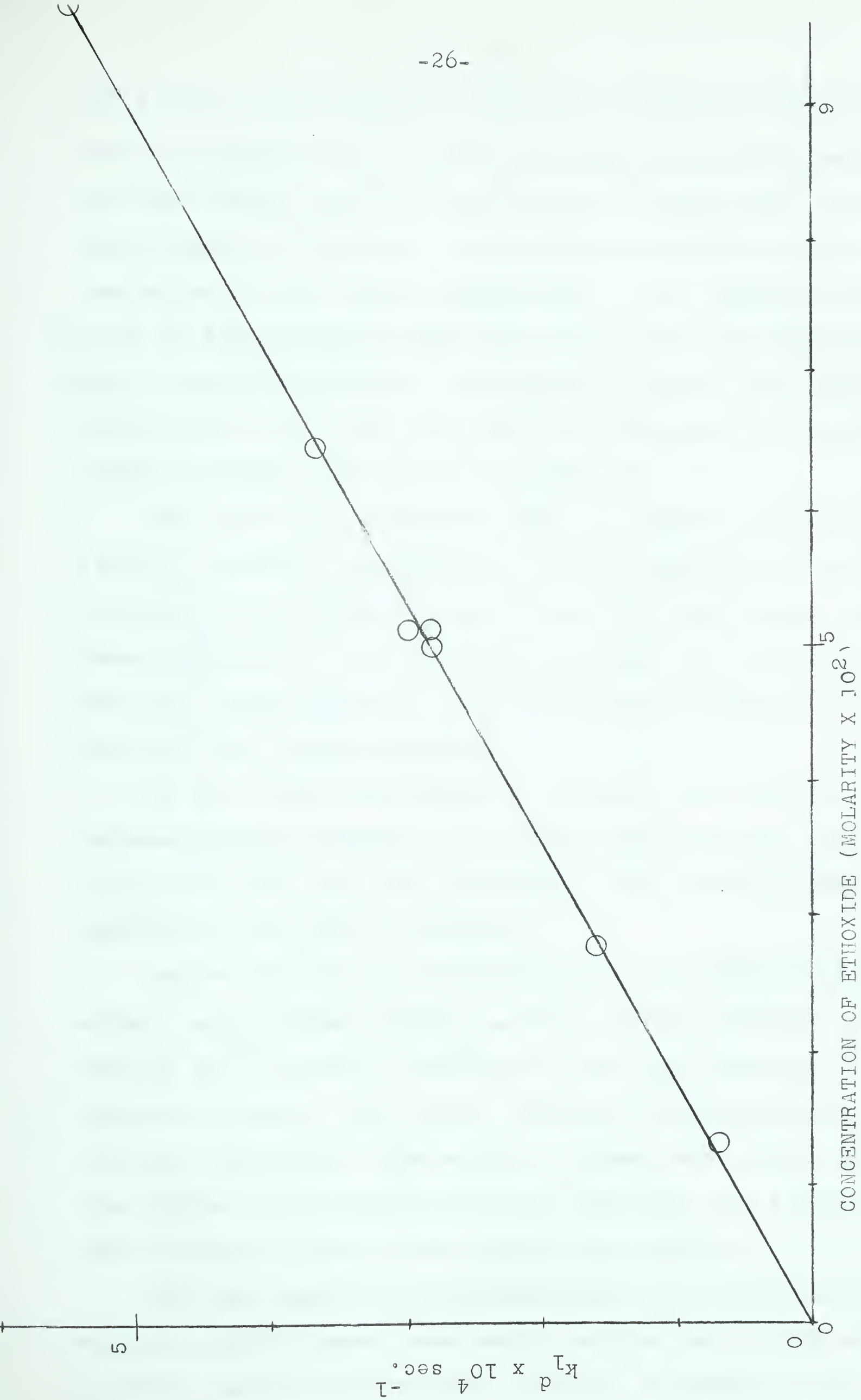


FIGURE 3: Plot of rate of disappearance of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) against concentration of ethoxide in 80% by vol. ethanol-water at 25°C.

and a plot of the rate data therein can be seen in Figure 2. The rate of disappearance of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) can be clearly seen to observe good first-order kinetics (Figure 2). First-order dependence on the concentration of base can be clearly seen if one examines rates 59 to 67 in Table VIII, in which the concentration of ethoxide underwent a tenfold variation. In Figure 3, a good linear correlation is obtained if one plots the rate of disappearance of ester (XXVII) against concentration of ethoxide.

The rate of appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII), however, was observed to drift downwards as reaction proceeded, due to slow decomposition of the ethyl ester under these conditions. An approximation to this rate was obtained from the initial slope of a plot of the data (Figure 2), before the drift had become appreciable.

To aid in the interpretation of these data, ethyl 2,6-dimethylbenzenesulfinate (XXXIII) was prepared independently, and was solvolysed under the same conditions. The results of this investigation are given in Table X.

Before studying the solvolysis of ester (XXVII) in 100% ethanol using sodium ethoxide as base, certain controls were carried out in order to determine if the base ethoxide, or the suspected product, ethyl ester (XXXIII), decomposed under the reaction conditions. The results of these tests (Table XII) show little or no reaction of these compounds over a period of 300 to 800 half lives of the parent ester (XXVII).

The rate studies on p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) were consequently carried out in 100% ethanol at 25°C., using sodium ethoxide as base. A summary of the data

- TABLE X -

SUMMARY OF RUNS CARRIED OUT ON ETHYL 2,6-DIMETHYLBENZENESULFINATE
(XXXIII) IN 80% by vol. ETHANOL WITH SODIUM ETHOXIDE AS BASE
AT 25°C.

Run	$[\text{EtO}^-] \text{ M}$	$[\text{Ester}] \text{ M}$	$k_1 \times 10^5 \text{ sec}^{-1}$	$k_2 \times 10^3 \text{ l/mole sec.}$	Lab. Book Ref.
45	0.05360	0.04093	3.93 ± 0.48	1.25 ± 0.26	147-2
50	0.05001	0.02489	5.71 ± 0.25	1.48 ± 0.10	149-2
51	0.04924	0.02506	5.19 ± 0.14	1.49 ± 0.03	225-1
58	0.05069	0.02510	5.51 ± 0.22	1.28 ± 0.08	245-1
62	0.05107	0.02506	5.64 ± 0.29	1.48 ± 0.05	259-1
63	0.05114	0.02487	5.89 ± 0.20	1.32 ± 0.08	263-1

Where k_1 is the first-order rate of disappearance of ethyl ester (XXXIII), and $k_2 = k_z$.

A sample rate, extracted from the above, together with a plot of the data contained therein, may be found in Table XI and Figure 4 respectively.

- TABLE XI -

RUN # 58 - THE SOLVOLYSIS OF ETHYL 2,6-DIMETHYLBENZENESULFINATE (XXXIII) IN 80% by vol.

ETHANOL-WATER WITH SODIUM ETHOXIDE AS BASE AT 25°C. $[\text{Ester}] = 0.02510\text{M}$; $[\text{EtO}] = 0.05069\text{M}$

$t_{\text{sec.}}$	m.l. Acid (b-x)	$\text{Log}(b-x)$	$\text{Log} \frac{I_0}{I}$ (a-x)	$\text{Log} \frac{a}{(a-x)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^5 \text{ sec.}^{-1}$	$k_2 \times 10^3 \text{ l/mole sec.}$
0	4.598	0.66257	1.23378	0.09124	--	--	--
900	4.415	0.64493	1.09504	0.03943	25.5	13.2	3.42
1800	4.282	0.63165	1.05049	0.02139	12.8	8.93	1.95
3375	4.108	0.61363	0.98823	1.99485	6.82	6.57	1.27
4800	3.868	0.58749	0.93327	1.97000	4.79	5.81	0.865
7515	3.739	0.57276	0.80448	1.90551	3.06	5.69	1.15
11760	3.396	0.53097	0.64501	1.80956	1.96	5.52	1.15
15000	3.232	0.50947	0.52720	1.72197	1.53	5.66	1.29
20460	3.117	0.49374	0.42456	1.62793	1.12	5.19	1.30
33480	2.815	0.44948	0.21882	1.34008	0.687	5.16	1.41
56040	2.514	0.40037	0.08814	2.94516	0.411	4.71	1.42

Acid = $[\text{HCl}] = 0.05253\text{M}$

(b-a) = 0.02559M Average $k_1 = 5.51 \pm 0.22 \times 10^{-5} \text{ sec.}^{-1}$

Average $k_2 = 1.28 \pm 0.08 \times 10^{-3} \text{ l/mole sec.}$

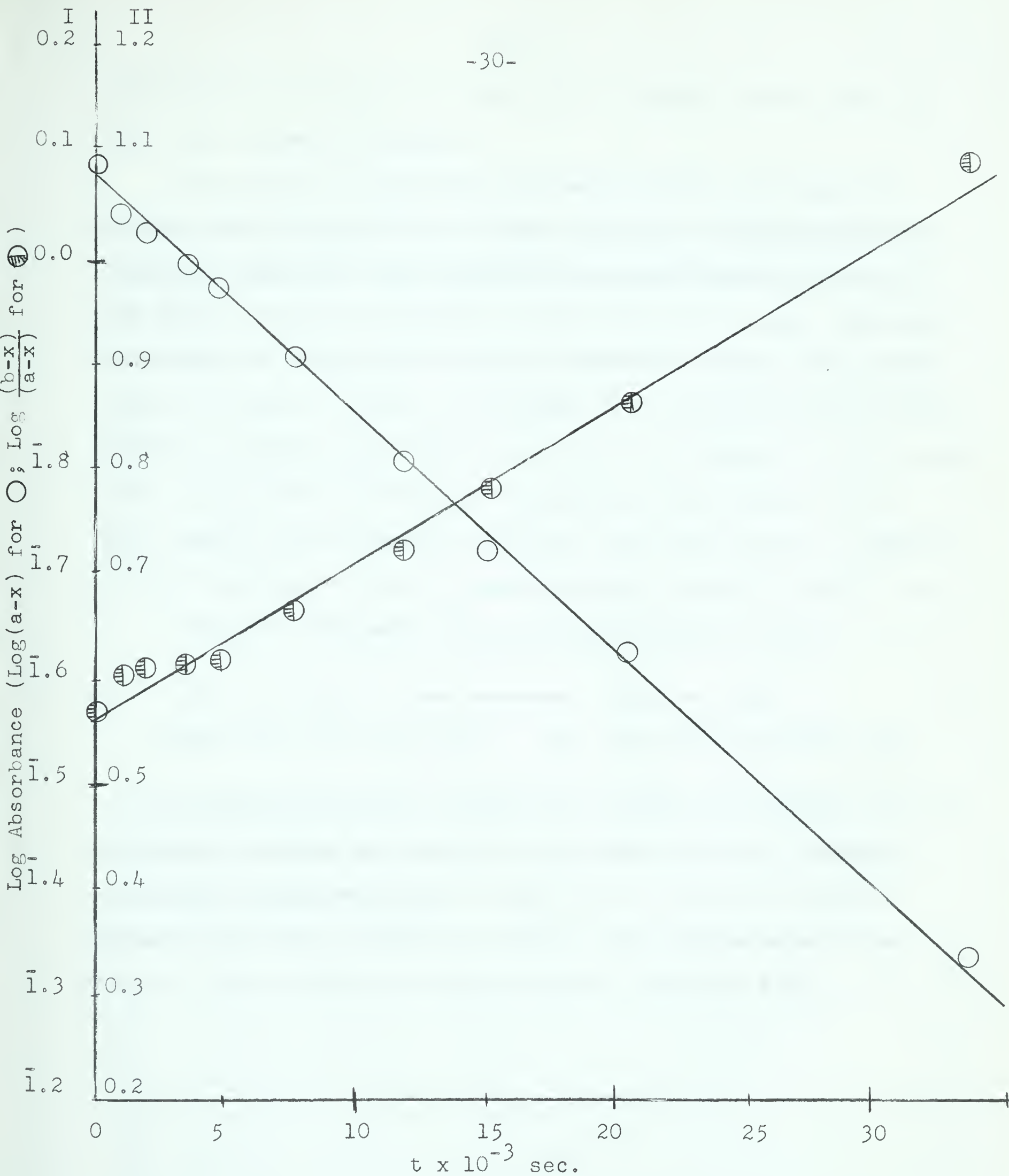


FIGURE 4: Plot of data from the solvolysis of ethyl 2,6-dimethylbenzenesulfinate (XXXIII) in 80% ethanol at 25°C. with sodium ethoxide as base (Run 58). I = \bigcirc ; II = \odot .

obtained is put forward in Table XIII, together with a plot of this rate, given in Figure 5.

The rate of disappearance of ester (XXVII), as measured by the rate of appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII), exhibited good pseudo-first-order kinetics since no net base consumption occurred in the over-all process. Although dependence on ethoxide ion was not tested by varying the concentration of base, one may, by analogy with the same system in 80% ethanol, presume that bimolecular attack by ethoxide ion on sulfur does occur, with the resultant expulsion of an alkoxide ion. This species would abstract a proton from the solvent to regenerate the ethoxide ion plus p-methoxyneophyl alcohol (XXXII). i.e.,



Where $\text{R}' = 2,6-(\text{CH}_3)_2\text{C}_6\text{H}_3-$ and $\text{R} = \text{p}-\text{OCH}_3\text{C}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2-$

In order to obtain a comparison between the previous results on primary systems and esters of secondary alcohols, isopropyl 2,6-dimethylbenzenesulfinate (XXXIV) was prepared by similar methods, and was solvolysed at 25°C., with sodium ethoxide as base in 100% and 80% by volume ethanol (see Table XVI).

- TABLE XII -

CONTROL RUNS ON THE DECOMPOSITION OF ETHYL 2,6-DIMETHYLBENZENE-SULFINATE (XXXIII) IN 100% ETHANOL WITH SODIUM ETHOXIDE AS BASE AT 25°C.

Run	$[\text{EtO}^-] \text{ M}$	$[\text{Ester}] \text{ M}$	% Base Consumed ^a	in T hrs.	Lab. Book Ref.
48	0.04978	--	3.0	234	217-1
49	0.04696	0.02488	3.4	234	219-1
52	0.05403	--	0.0	145	229-1
53	0.05418	--	2.8	98	229-1

a- % Base consumption = % loss of titer of base solution.

- TABLE XIII -

SUMMARY OF DATA FROM THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) IN 100% ETHANOL WITH SODIUM ETHOXIDE AS BASE AT 25°C.

Run	$[\text{EtO}^-] \text{ M}$	$[\text{Ester}] \text{ M}$	$k_1 \times 10^4 \text{ sec}^{-1}$	$k_1 / [\text{EtO}^-] \times 10^2 \text{ l/mole sec.}$	Lab. Book Ref.
42	0.04509	0.02449	5.07 ± 0.23	1.12	191-1
43	0.04545	0.02429	5.34 ± 0.18	1.17	195-1
54	0.04820	0.02402	5.98 ± 0.27	1.24	235-1
55	0.04871	0.02417	6.23 ± 0.13	1.28	239-1
60	0.04856	0.02420	6.09 ± 0.24	1.25	249-1
115	0.02602	0.02540	3.24 ± 0.07	1.25	187-2

- TABLE XIV -

RUN # 60- THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) IN 100%

ETHANOL WITH SODIUM ETHOXIDE AS BASE AT 25°C. $[\text{Ester}] = 0.02420\text{M}; [\text{EtO}^-] = 0.04856\text{M}$						
$t_{\text{sec.}}$	ml. Acid	$\text{Log } \frac{I_0}{I}$ (a-x)	Log (a-x)	$\text{Log } \frac{a}{(a-x)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^4 \text{ sec.}^{-1}$
0	4.490	1.11236	0.04625	--	--	--
330	4.456	0.86606	1.93754	0.10871	69.79	7.61
720	4.430	0.72125	1.85808	0.18817	31.99	6.02
1080	4.389	0.59384	1.77366	0.27259	21.32	5.82
2070	4.426	0.29976	1.47676	0.56949	11.13	6.33
2910	4.384	0.17457	1.23196	0.81429	8.00	6.52
3800	4.384	0.10395	1.01682	1.02943	6.09	6.27
4680	4.379	0.06914	2.83972	1.20653	4.92	5.93
5640	4.385	0.04352	2.63868	1.40757	4.08	5.74

Acid $[\text{HCl}] = 0.05253\text{M}$

Here, k_1 is the rate of disappearance of

ester (XXVII).

Average $k_1 = 6.09 \pm 0.24 \times 10^{-4} \text{ sec.}^{-1}$

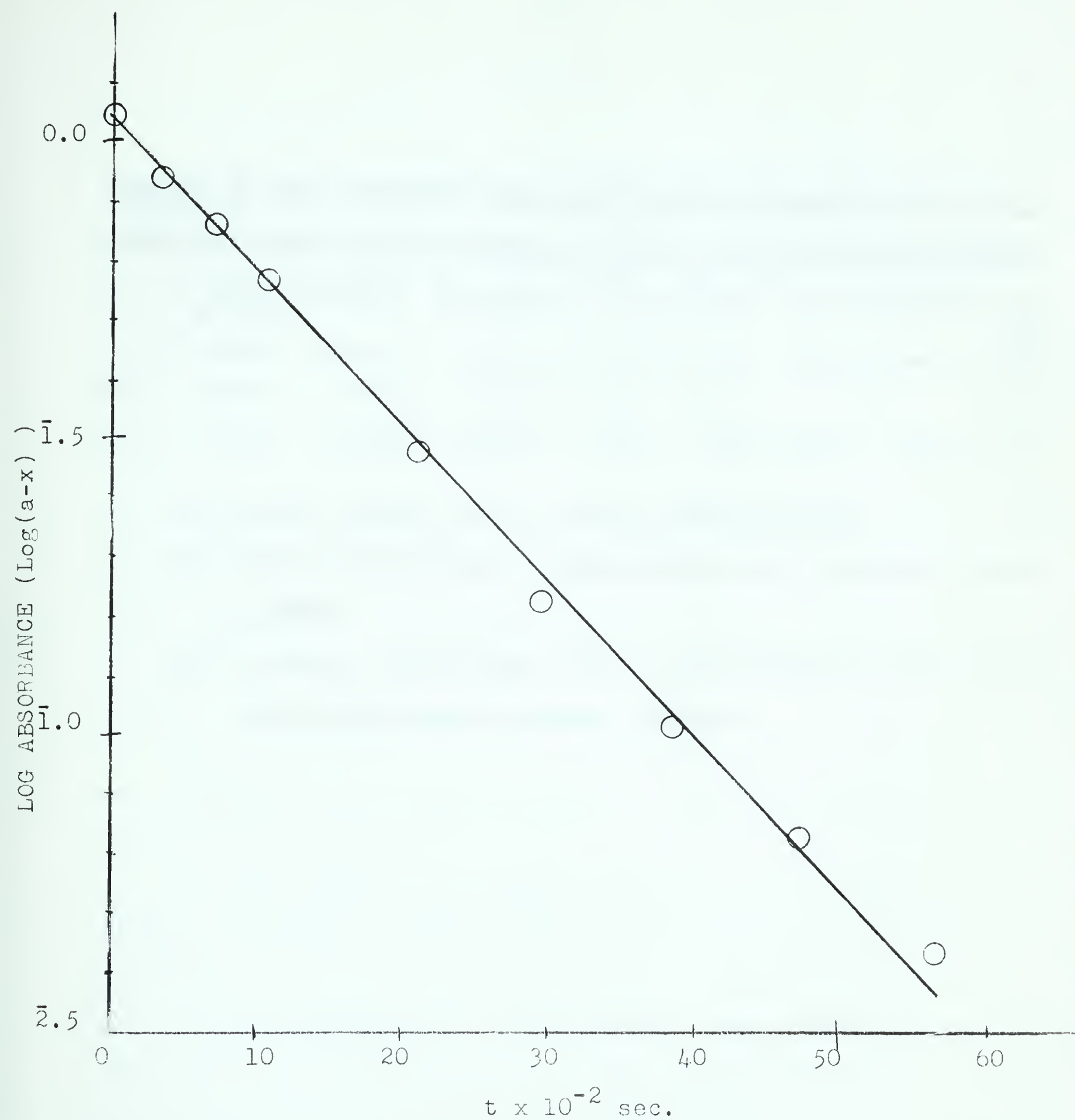


FIGURE 5: Plot of decrease in concentration of ester against time for the solvolysis of *p*-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) in 100% ethanol with sodium ethoxide as base at 25°C. (Run 60).

SUMMARY OF RATE CONSTANTS FOR THE REACTION OF ISOPROPYL 2,6-DI-METHYLBENZENESULFINATE (XXXIV) AT 25° C. USING ETHOXIDE AS BASE.

Run	Solvent ^a % EtOH	[EtO] M	[Ester] M	$k_1^d \times 10^4 \text{sec.}^{-1}$	$k_1^a \times 10^4 \text{sec.}^{-1}$	Lab. Book Ref.
69	100	0.04549	0.02537	2.21 0.06	----	285-1
68	80	0.04854	0.02555	0.935 0.025	0.607 0.020	152-2

a- Solvent refers to % by volume ethanol-water.

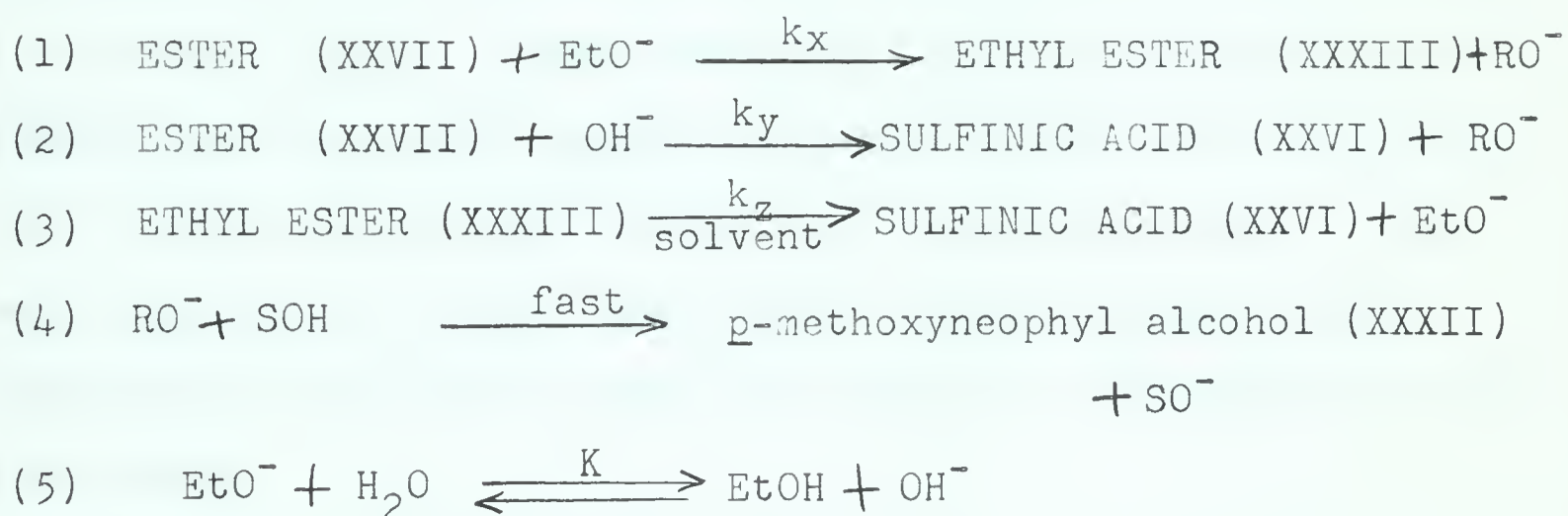
k_1^d First-order rate of disappearance of isopropyl ester (XXXIV).

k_1^a Initial first-order rate of appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII).

PART II

DISCUSSION

Examination of the foregoing data, taken together with the data obtained in the titrimetric rates and product runs in the preceding section, would lead one to the initial formulation of the following scheme of reaction for p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) in 80% ethanol with sodium ethoxide as base:



where $\text{R} = \text{p-OCH}_3\text{C}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2-$ and $\text{SOH} = \text{solvent}$

In ester (XXVII), attack by ethoxide or hydroxide ion can occur on sulfur to produce ethyl 2,6-dimethylbenzenesulfinate (XXXIII) or 2,6-dimethylbenzenesulfinic acid (XXVI), by paths (1) or (2) respectively. Since neither steps (1) nor (4) produce acid, the slow decrease in base titer observed in this medium can be attributed to (2) and/or (3).

The possibility of attack by either of two different nucleophilic species on ester (XXVII) is evident from equation (5). However, comparison of the rate of disappearance of ester (XXVII), k_1^d , with the initial rate of formation of ethyl ester (XXXIII), k_1^a , in Table VIII, indicated the two rates to be approximately equal. This would mean that in the above scheme,

$k_x \lesssim k_1^a$, and that k_x would be considerably larger than k_y . Therefore this would indicate that ethoxide ion is more nucleophilic towards sulfur than is hydroxide ion and consequently, the importance of equation (2) in the overall scheme would be minimal.

It is evident, on examination of the rate of formation of ethyl 2,6-dimethylbenzenesulfinate (XXXIII), in run 61, (Table IX, Figure 2), that this material underwent decomposition under the reaction conditions. However, this process occurs at such a rate that $k_x \gg k_z$, since a definite build-up of ethyl ester (XXXIII) was observed during the initial stages of the solvolysis. Such second-order consecutive reactions result in kinetic expressions of much complexity, unless certain approximations can be made to bring the system to a kinetically solvable state.

Fortunately, ethyl ester (XXXIII) may be prepared and solvolysed under the same reaction conditions (Table X). It is evident from this data that the rate of disappearance of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) is only about five to six times faster than the rate of disappearance of ethyl ester (XXXIII). Consequently, this reaction sequence cannot be dissected since the resultant parts could not be treated as two separate second-order processes.

In 100% ethanol, isopropyl 2,6-dimethylbenzenesulfinate (XXXIV) solvolysed readily to give ethyl ester (XXXIII), as one would expect, at a rate which was slightly slower than the primary system, p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII). This factor of 2.4 decrease in rate (compare runs 68 and 43 in Tables XVI and XIII respectively), for a

secondary system, in comparison with a primary, may be explained by the poorer nature of the leaving group in the displacement on sulfur by ethoxide ion. In the above case, we have expulsion of a secondary isopropoxide ion as compared with the primary ion liberated in the solvolysis of p-methoxyneophyl-2,6-dimethylbenzenesulfinate (XXVII).

Isopropyl 2,6-dimethylbenzenesulfinate (XXXIV) behaves in much the same manner as does ester (XXVII) in 80% by volume ethanol-water. Displacement by hydroxide ion on sulfur, however, seems to have become more significant in this case. This fact may be illustrated by examination of the k_1^d/k_1^a ratios for these two compounds.

PART III

The Effect of Other Nucleophiles on Sulfur-Oxygen Bond FissionRESULTS

A re-investigation was undertaken, at this time, of the solvolysis of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) in 100% ethanol, using acetate ion or 2,6-lutidine as base. Potassium acetate was used here, in place of the corresponding sodium salt, since it proved to be far more soluble in 100% ethanol. The infrared method of rate investigation was again employed so that both disappearance of ester (XXVII) and appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII) could be followed simultaneously. A summary of the data obtained is presented in Table XVII. All rate constants contained therein were calculated from the rate of formation of ethyl ester (XXXIII) except in the case of runs 95 and 96, which were carried out in 60% by vol. ethanol-water. Here, rate of disappearance of ester (XXVII) was used since the ethyl ester decomposed readily, under the reaction conditions, on formation.

Since p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) proved to be quite unreactive when 2,6-lutidine was used as base, a theoretical infinity was utilized in calculating the approximate rate constants given below. This value corresponded to a concentration of ethyl 2,6-dimethylbenzenesulfinate (XXXIII) which would result from a 100% conversion of ester (XXVII). An approximation to this number was obtained from a Lambert-Beer plot of concentration vs. absorbance (i.e., $\log \frac{I_0}{I}$) for ethyl ester (XXXIII).

All the runs below, carried out using potassium acetate as

- TABLE XVII -

SUMMARY OF RUNS CARRIED OUT ON p-METHOXYNEOPHYL 2,6-DIMETHYL-
BENZENESULFINATE (XXVII) IN 100% ETHANOL AT 90°C.

Run	Base	[Base] M	[Ester] M	$k_1^a \times 10^5 \text{ sec.}^{-1}$	$k_1 / [\text{OAc}^-] \times 10^4 \text{ l./mole sec.}$	Lab. Book Ref.
75	KOAc	0.04990	0.02410	0.657	1.31	171-2
80	"	0.04776	0.02422	0.746	1.56	173-2
93	"	0.04776	0.02415	0.867	1.43	175-2
94	"	0.03184	0.02466	0.600	1.88	177-2
96 ^b	"	0.05730	0.02526	0.047	--	81-2
97	"	0.09552	0.02462	1.64	1.71	179-2
74	2,6-Lutidine	0.05050	0.02466	0.00061		11-2
91 ^c	"	0.05086	0.02424	0.0160 ± 0.0015		63-2
95 ^b	"	0.06043	0.02494	0.0072		79-2
102 ^d	"	0.05086	0.02455	0.286 ± 0.017		113-2
77	C ₅ H ₅ N	0.05124	0.02410	0.013		17-2

a- All rates measured from appearance of ethyl 2,6-dimethylbenzenesulfinate (XXXIII) unless otherwise specified.

b- Runs carried out in 60% by vol. ethanol-water and followed from the rate of disappearance of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII).

c- Run carried out with added salt. $[\text{KSCN}] = 0.05844\text{M}$.

d- " " " " " " . $[\text{LiN}_3] = 0.04450\text{M}$.

base, exhibited a substantial upward drift in rate constant as the reaction proceeded. This fact can be seen by examination of a sample run (run 80) in Table XVIII and a plot of the data contained therein in Figure 6. This drift was apparent if either p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) disappearance or ethyl 2,6-dimethylbenzenesulfinate (XXXIII) appearance was measured. The rate constants presented in Table XVIII were obtained from an initial slope of the curve obtained on plotting $\log(D_{\infty} - D)$ against time, before the curvature had become appreciable (see Figure 6). A reasonably linear relationship was obtained on plotting this initial k_1 against acetate concentration (Figure 7).

When 2,6-lutidine was used as base, the solvolysis proceeded extremely slowly in comparison with those runs carried out with added potassium acetate (k_1 formation of ethyl ester (XXXIII) $6 \times 10^{-9} \text{ sec}^{-1}$).

In addition, rates were carried out on the same compound using 2,6-lutidine as base with added nucleophilic salts such as potassium thiocyanate and lithium azide (Table XVI). In both cases, ethyl ester (XXXIII) was the only sulfur-bearing product. Examination of the products by infrared spectroscopy, as reaction proceeded, showed no sign of the unstable intermediate thiocyanate or azide (i.e., $\text{R}-\overset{\text{O}}{\underset{\text{O}}{\text{S}}}-\text{SCN}$ or $\text{R}-\overset{\text{O}}{\underset{\text{O}}{\text{S}}}-\text{N}_3$ respectively).

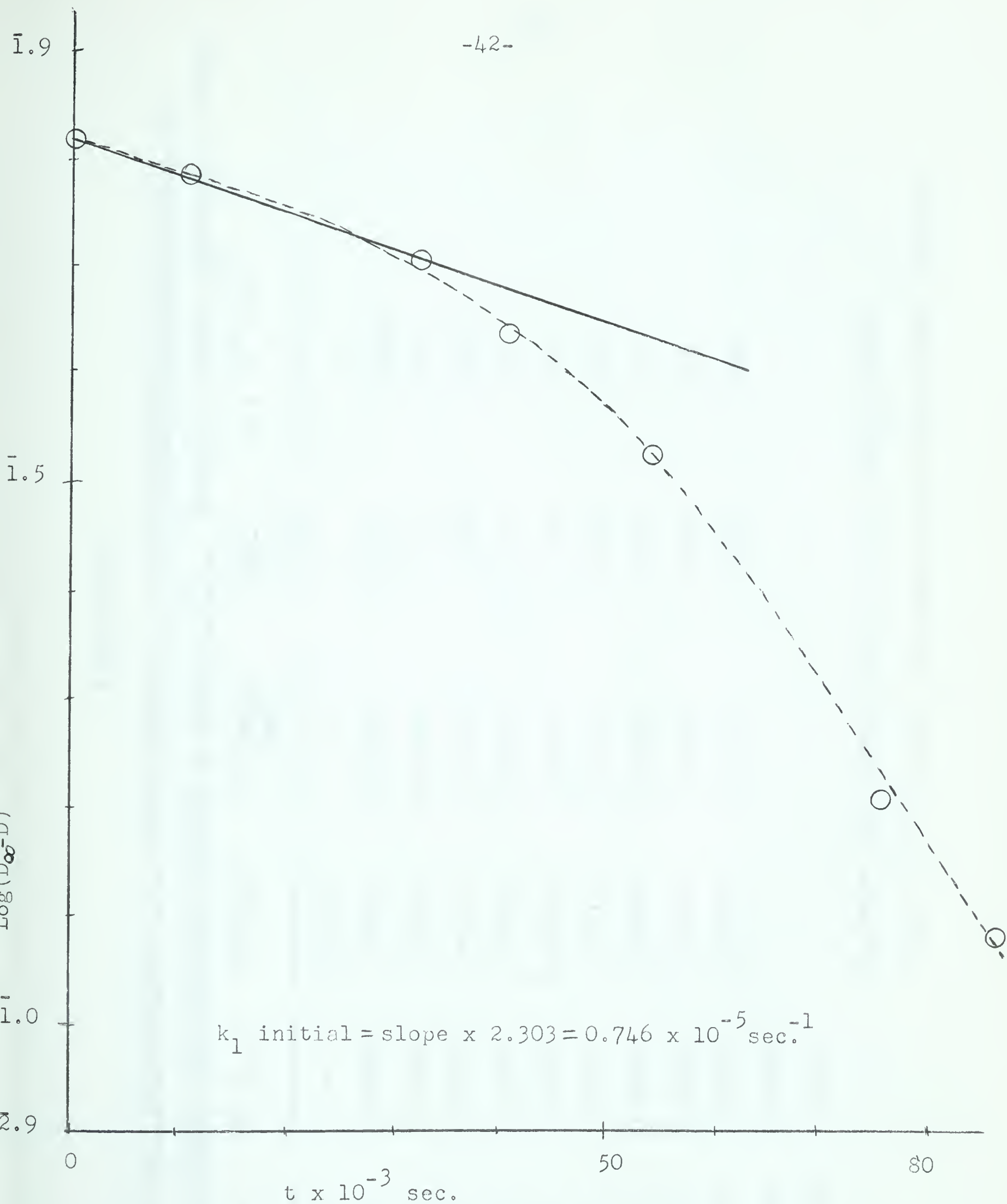


FIGURE 6: Plot of data obtained for the solvolysis of *p*-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) in 100% ethanol with potassium acetate as base, at 90°C. (Run 80 - Table XVIII).

[ester] = 0.02422M ; [acetate] = 0.04776M

- TABLE XVIII -

RUN # 80 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII) IN 100% ETHANOL WITH POTASSIUM ACETATE AS BASE AT 90°C. $[\text{Ester}] = 0.02422\text{M}$; $[\text{Acetate}] = 0.04776\text{M}$

t sec.	$\text{Log } \frac{I_0}{I} = D$	$\text{Log}(D_\infty - D)$	$\text{Log} \left(\frac{D_\infty - D_0}{D_\infty - D} \right)$	$\frac{2.303}{t} \times 10^5$	$k_1 \times 10^6 \text{ sec.}^{-1}$
0	---	1.81624	---	--	--
10800	0.04275	1.78675	0.02949	21.32	0.628
32400	0.13919	1.71265	0.10359	7.11	0.736
40500	0.21708	1.64147	0.17477	5.69	0.996
54000	0.31491	1.53148	0.28476	4.27	1.22
75600	0.49330	1.20952	0.60672	3.05	1.85
86760	0.53547	1.07918	0.73706	2.65	1.95
97380	0.56212	2.96848	0.84776	2.37	2.01
124680	0.60356	2.70757	1.10867	1.85	2.05
182340	0.63231	2.36173	1.45451	1.26	1.83
8 days	0.53678				
65 days	0.38957				

T_∞ taken from Lambert-Beer control = $\text{Log } \frac{I_0}{I} = 0.655$

Here, k_1 is the rate of appearance of ethyl ester (XXXIII)

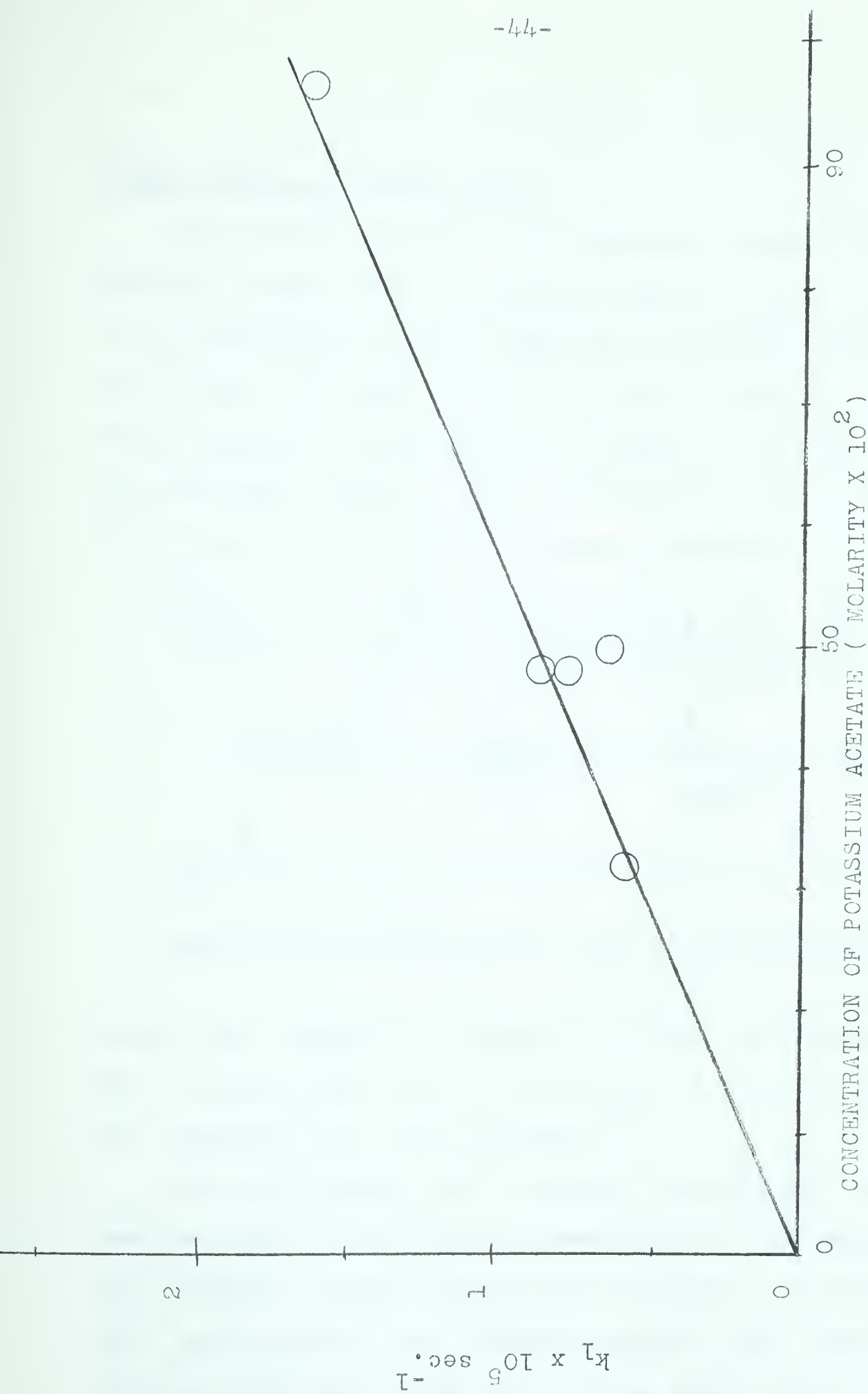
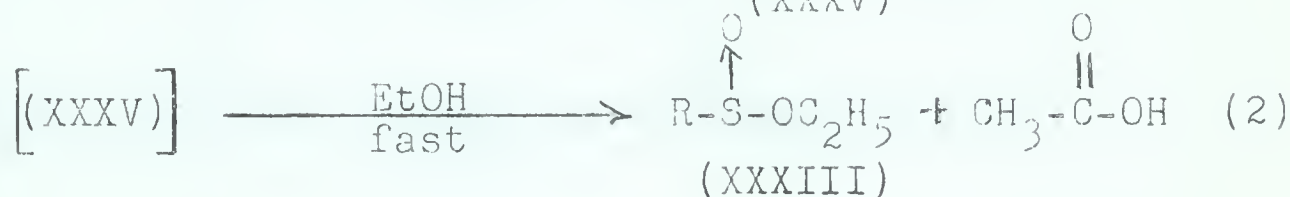
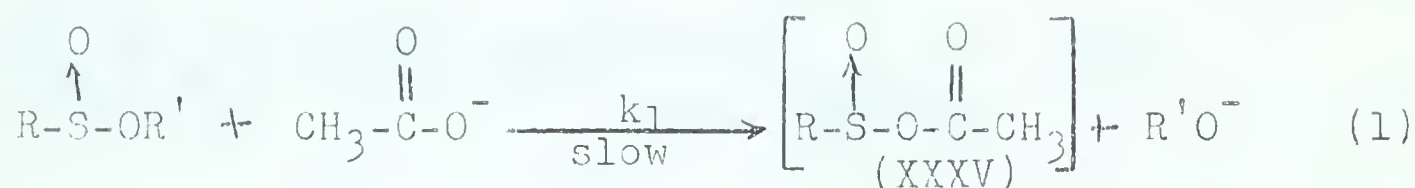


FIGURE 7: Plot of dependence of initial k_1 on concentration of potassium acetate in the solvolysis of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) in 100% ethanol at 90°C. The data plotted was obtained from Table XVII.

DISCUSSIONi) The effect of weaker bases

The results obtained, with potassium acetate as base, would tend to suggest that a process, similar to that which occurred with ethoxide ion in 100% ethanol, was taking place here. Attack by acetate ion would presumably occur on sulfur to give the highly unstable mixed anhydride (XXXV), by a rate determining second-order process. This intermediate would then quickly solvolyse to give ethyl 2,6-dimethylbenzenesulfinate (XXXIII).



Where $\text{R} = 2,6-(\text{CH}_3)_2\text{C}_6\text{H}_3-$; and $\text{R}' = p\text{-OCH}_3\text{C}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2-$

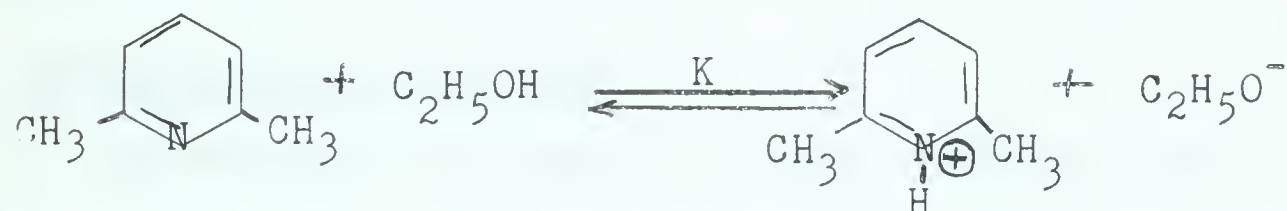
Since equal amounts of alkoxide and acid are produced, the acetate ion is regenerated and no net change in titer is observed during the reaction (i.e., see Equation 3).

The large upward drift in rate, as reaction proceeded, has been ascribed to the slow decomposition of the ethyl ester product (XXXIII) formed during the solvolysis. The existence of this decomposition only becomes apparent when sulfur-oxygen bond cleavage has been slowed down to the extent where the two processes proceed at comparable rates, as in the case of ester (XXVII).

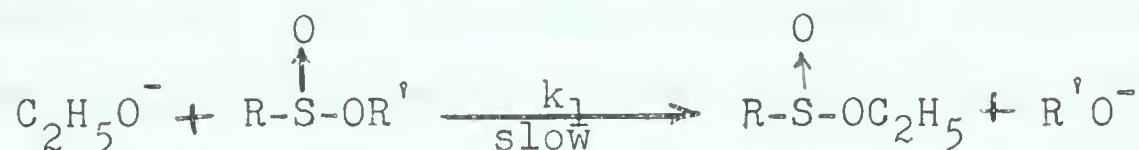
This is not at once apparent in such systems. However, examination of an infinity point in run 80 (see Table XVIII), which had been left in the bath for an extended period of time (65 days), showed that 40% of the ethyl ester product had been consumed.

With respect to those rates carried out on p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) using 2,6-lutidine as base, two possible modes of reaction can be postulated to account for the formation of ethyl 2,6-dimethylbenzenesulfinate (XXXIII):

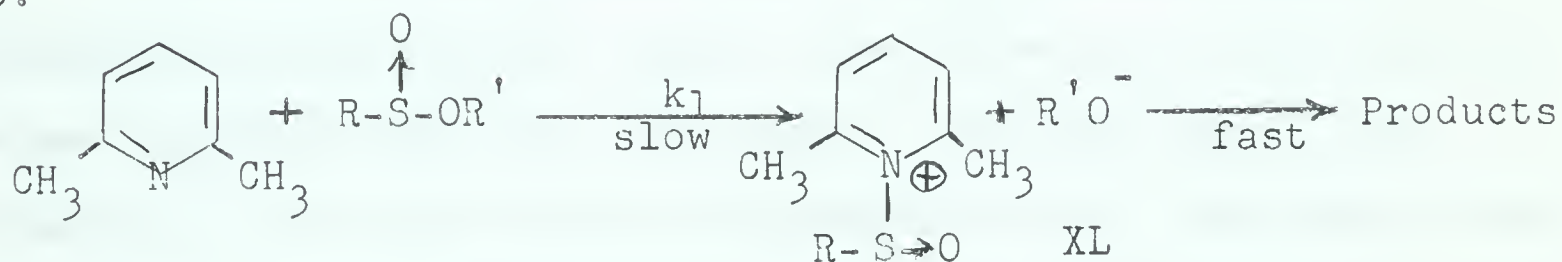
4a.



4b.



5.



In equation 4a, K would presumably lie far to the left, such that a very small amount of ethoxide ion would be present to accomplish the displacement. In equation 5, the 2,6-lutidine itself would act as nucleophile, to form an unstable intermediate such as XL, as in the case of the acetate runs, which would undergo quick solvolysis to products.

If one carried out a run on p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) under the same conditions as above,

using pyridine as base, equation 4 would predict a slower rate of solvolysis since pyridine, being a weaker base than 2,6-lutidine, would result in a lower equilibrium concentration of ethoxide ion. If system 5 was operable, then, one would predict that the sterically less hindered pyridine would give rise to a faster displacement reaction.

Run 77 (Table XVII) would seem to rule out equation 4 and favor the second pathway. In these experiments, however, one cannot rule out the possibility that the solvent might carry out the displacement itself.

ii) The effect of solvent

By varying the polarity of the medium in which a solvolysis is carried out, one may predict what effect the change will have on the rate, if one examines the corresponding effect on solvation of the transition state⁴¹.

In the reaction of acetate ion with p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII), the formation of the unstable mixed anhydride has been postulated. In such a case, (the reaction of an ion with an uncharged molecule), the charge density on the acetate ion is dispersed over a somewhat larger area in the transition state. Consequently, one would predict that an increase in polarity of the medium would tend to disfavor the formation of the mixed anhydride, and a consequent decrease in rate should be observed. This is, indeed, what was found. On going from 100% to 60% by vol. ethanol-water, the rate had decreased by a factor of about 15 (Table XVII).

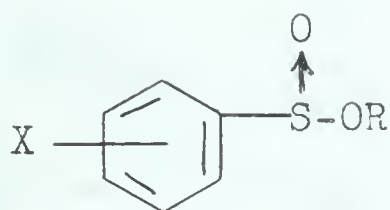
Similarly, if one proceeds from two uncharged species to form a charged intermediate, an increase in polarity of the

medium should favor the reaction. The runs carried out in the presence of 2,6-lutidine verify this assumption (see discussion page 42 and Table XVII). On going from 100% to 60% by vol. ethanol-water, one observed a 12-fold increase in rate.

PART IV

THE EFFECT OF SUBSTITUENTS ON SULFUR-OXYGEN BOND CLEAVAGE

In order to investigate the effect which different substituents on the sulfinic group would have on the rate of sulfur-oxygen bond cleavage, 2-chloro and 2-methylbenzenesulfinic acids were prepared by the method used previously for the preparation of 2,6-dimethylbenzenesulfinic acid (XXVI) (see P.9). Zinc reduction of p-toluenesulfonyl and benzenesulfonyl chlorides afforded 4-methyl and unsubstituted benzenesulfinic acids respectively. The corresponding p-methoxyneophyl esters were prepared as previously described (see p. 10).



Where $R = \text{p-CH}_3\text{OC}_6\text{H}_4\text{C}(\text{CH}_3)_2\text{CH}_2-$
and $X = \text{H-}$ (XXXVI)

2- CH_3- (XXXVII)

4- CH_3- (XXXVIII)

2- Cl- (XXXIX)

Since rate of formation of the corresponding ethyl ester, followed by infrared spectroscopy, had proven to be the more facile method of following the solvolysis of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII), the preparation of the corresponding ethyl esters of the above substituted sulfinic acids was carried out. These compounds were found to obey the Lambert-Beer law over the concentration range studied, and they could be isolated in a consistent manner from the reaction mixture, by the pentane extraction procedure utilized earlier.

-TABLE XIX -

SUMMARY OF DATA ON THE SOLVOLYSIS OF p-METHOXYNEOPHYL BENZENE-SULFINATE (XXXVI) IN 100% ETHANOL AT 90°C.

Run	Base	[Base] M	[Ester] M	$k_1 \times 10^4 \text{ sec}^{-1}$	$k_1 / [\text{OAc}] / \text{mole sec.}$	Lab. Book Ref.
71 ^a	KOAc	0.04990	0.02468	2.18 ± 0.26	4.37	3-2
72 ^a	"	0.04990	0.02461	2.57 ± 0.10	5.14	7-2
	Rate of formation of ethyl ester			2.72 ± 0.17	5.45	
81	"	0.04776	0.02502	2.78 ± 0.17	5.82	29-2
82	"	0.03184	0.02528	1.96 ± 0.10	6.15	31-2
83	"	0.01592	0.02564	1.07 ± 0.07	6.72	35-2
86	"	0.07970	0.02508	4.81 ± 0.15	6.04	41-2
70	2,6-Lutidine	0.05050	0.02552	0.00022		293-1
79	"	0.05036	0.02422	0.00077 ± 0.000064		23-2
105 ^b	"	0.05036	0.02479	2.08 ± 0.06		123-2
78	C ₅ H ₅ N	0.05424	0.02464	0.0123 ± 0.0021		21-2

a- Rate followed by measurement of disappearance of ester (XXVII).

b- Run carried out in the presence of $[\text{LiN}_3] = 0.1113\text{M}$.

All runs, unless otherwise specified, were followed by measurement of the appearance of the corresponding ethyl ester. A theoretical infinity, taken from a Lambert-Beer law plot for the ethyl ester, was used in the calculation of a rate constant for runs 70 and 79.

- TABLE XX -

RUN # 81 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL BENZENESULFINATE (XXXVI) IN 100% ETHANOL

AT 90°C. WITH POTASSIUM ACETATE AS BASE. [Ester] = 0.02502M ; [Acetate] = 0.04776M

$t_{\text{sec.}}$	$\text{Log } \frac{I_0-D}{I}$	$\text{Log}(D_\infty-D)$	$\text{Log} \frac{(D_\infty-D_0)}{(D_\infty-D)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^4 \text{ sec.}^{-1}$
0	0.01391	1.89876	--	--	--
360	0.08640	1.85707	0.04169	63.97	2.67
660	0.16093	1.80959	0.08917	34.89	3.11
960	0.21639	1.77054	0.12822	23.99	3.08
1500	0.29908	1.70491	0.19385	15.35	2.98
1860	0.34657	1.66219	0.23657	12.38	2.93
2100	0.35441	1.65472	0.24402	10.97	2.68
2700	0.41944	1.58718	0.31158	8.53	2.66
3300	0.45820	1.54129	0.35747	6.98	2.49
3900	0.52871	1.44289	0.45587	5.91	2.70
4860	0.58498	1.34437	0.55439	4.74	2.63
6000	0.64167	1.21564	0.68312	3.84	2.62

10 hrs. 0.82304

Average = 0.80597 taken as T_∞

24 hrs. 0.78890

Average $k_1 = 2.78 \pm 0.17 \times 10^{-4} \text{ sec.}^{-1}$

where k_1 is the rate of appearance of the corresponding ethyl ester.

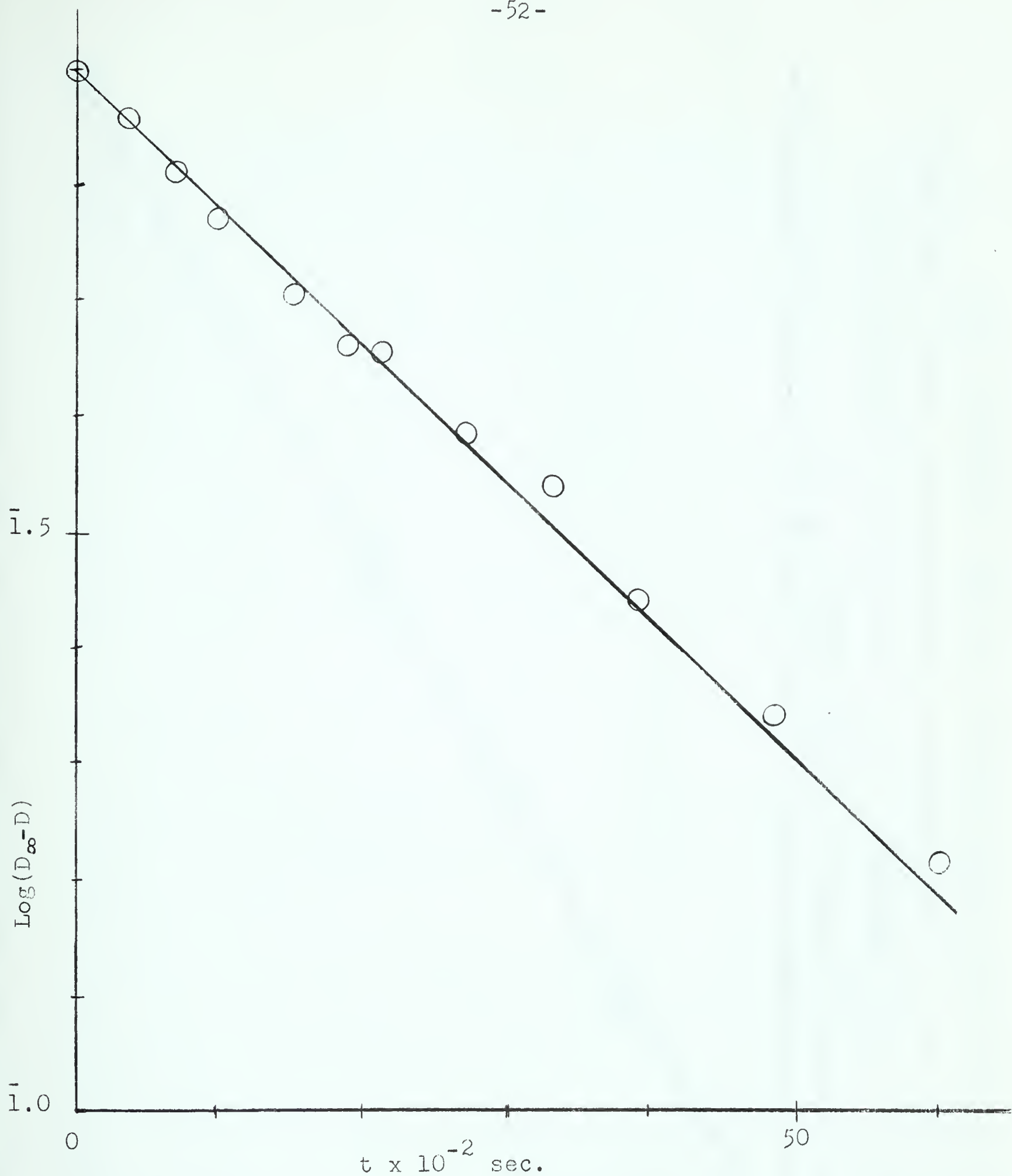


Figure 8: Plot of data for the solvolysis of *p*-methoxyneophyl benzenesulfinate (XXXVI) in 100% ethanol at 90°C. with potassium acetate as base(Run 81). $[\text{Ester}] = 0.02502\text{M}$; $[\text{KOAc}] = 0.04776\text{M}$.
 k_1 from plot = Slope $\times 2.303 = 2.72 \times 10^{-4} \text{ sec}^{-1}$.

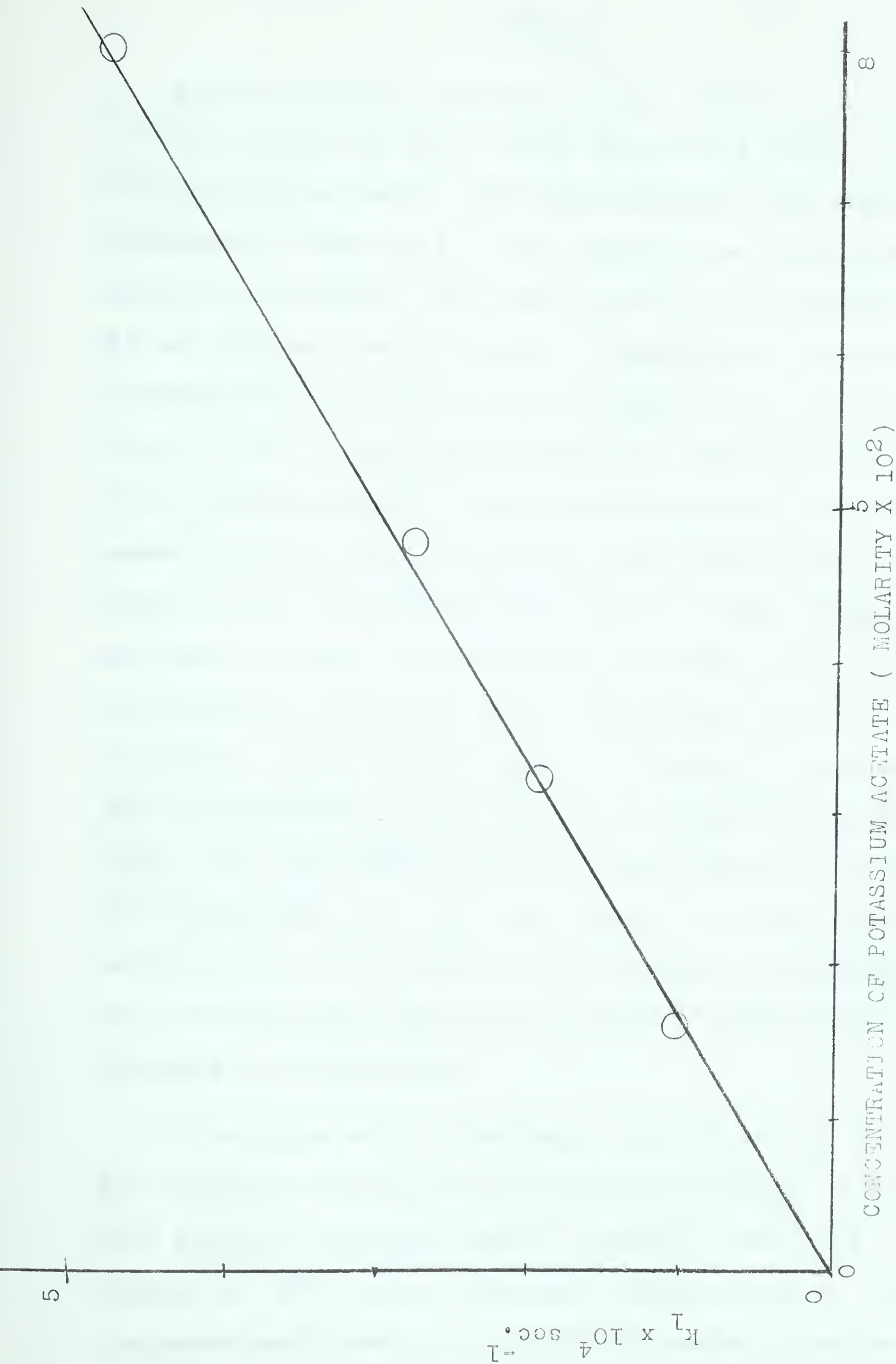


FIGURE 9: Plot of dependence of k_1 on concentration of potassium acetate in the solvolysis of p-methoxyneophyl benzenesulfinate (XXXVI) in 100% ethanol at 90°C. The data plotted was obtained from runs 81-86 (Table XIX).

RESULTS

p-Methoxyneophyl benzenesulfinate (XXXVI) was solvolysed in 100% ethanol at 90°C. using potassium acetate, 2,6-lutidine and pyridine as bases. The data obtained from these runs are presented in Table XIX. Good pseudo-first-order kinetics were observed throughout (see sample rate and plot thereof in Table XX and Figure 8 respectively). Dependence of rate on acetate concentration is illustrated in Figure 9 by a plot of data from runs 81 - 86. A similar situation to that which was observed with p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) seems to occur here, with those rates carried out with organic bases, i.e., 2,6-lutidine or pyridine. When potassium acetate was used as base, the solvolysis proceeded about 3000 times faster than in the case where 2,6-lutidine was utilized. Similarly, pyridine was found to be about 15 times more efficient at promoting sulfur-oxygen bond fission than was 2,6-lutidine. The run carried out with added azide ion in the presence of 2,6-lutidine (run 105) again shows the vast superiority of azide ion over 2,6-lutidine as nucleophile and gives a measure of the ability of azide ion to promote sulfur-oxygen bond cleavage in such systems.

A few rates were subsequently carried out on the 2-methyl, the 4-methyl and the 2-chlorobenzenesulfates of p-methoxyneophyl alcohol (compounds XXXVII, XXXVIII, and XXXIX), in 100% ethanol at 90°C., using potassium acetate as base. All three compounds exhibited good pseudo-first-order kinetics of solvolysis. Similarly, a plot of acetate concentration versus the rate of formation of ethyl ester(k_1), for each ester, showed a

- TABLE XXI -

SUMMARY OF DATA ON THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2-METHYL-BENZENESULFINATE (XXXVII) IN 100% ETHANOL AT 90°C. WITH POTASSIUM ACETATE AS BASE.

Run	[Ester] M	[Acetate] M	$k_1 \times 10^4 \text{ sec}^{-1}$	$k_1 / [\text{OAc}^-] \times 10^3 \text{ l/mole sec.}$	Lab. Book Ref.
90	0.02510	0.04776	1.15 ± 0.03	2.41	61-2
92	0.02571	0.04776	1.19 ± 0.03	2.49	65-2
106	0.02564	0.07786	1.59 ± 0.11	2.04	125-2
107	0.02493	0.03893	0.869 ± 0.052	2.23	129-2
112	0.02414	0.07786	1.68 ± 0.08	2.16	167-2

- TABLE XXII -

SUMMARY OF DATA ON THE SOLVOLYSIS OF p-METHOXYNEOPHYL 4-METHYL-BENZENESULFINATE (XXXVIII) IN 100% ETHANOL AT 90°C. WITH POTASSIUM ACETATE AS BASE.

Run	[Ester] M	[Acetate] M	$k_1 \times 10^4 \text{ sec}^{-1}$	$k_1 / [\text{OAc}^-] \times 10^3 \text{ l/mole sec.}$	Lab. Book Ref.
85	0.02535	0.04776	1.74 ± 0.15	3.65	39-2
87	0.02465	0.04776	1.60 ± 0.07	3.35	45-2
108	0.02523	0.03893	1.39 ± 0.03	3.58	133-2
110	0.02508	0.07786	3.13 ± 0.20	4.02	141-2
111	0.02372	0.11679	5.37 ± 0.26	4.60	165-2

- TABLE XXIII -

SUMMARY OF DATA ON THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2-CHLORO-
BENZENESULFINATE (XXXIX) IN 100% ETHANOL AT 90°C. WITH POTASSIUM
ACETATE AS BASE.

Run	[Ester] M	[Acetate] M	$k_1 \times 10^4 \text{ sec.}^{-1}$	$k_1 / [\text{OAc}] \times 10^3$ 1/mole sec.	Lab. Book Ref.
98	0.02486	0.04776	4.05 ± 0.25	8.48	89-2
99	0.02492	0.07960	6.55 ± 0.33	8.23	91-2
103	0.02502	0.03893	3.25 ± 0.17	8.36	117-2
104	0.02500	0.01946	1.89 ± 0.09	9.70	119-2

- TABLE XXIV -

RUN # 92 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2-METHYLBENZENESULFINATE (XXXVII) IN 100%

ETHANOL AT 90°C. WITH POTASSIUM ACETATE AS BASE. $[\text{Ester}] = 0.02571\text{M}$; $[\text{Acetate}] = 0.04776\text{M}$

$t_{\text{sec.}}$	$\text{Log } \frac{I_0-D}{I}$	$\text{Log}(D_\infty-D)$	$\text{Log} \frac{(D_\infty-D_0)}{(D_\infty-D)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^4 \text{ sec.}^{-1}$
0	--	1.85560	--	--	--
960	0.07918	1.80479	0.05081	23.99	1.22
2700	0.19837	1.71498	0.14062	8.53	1.20
3600	0.24999	1.66946	0.18614	6.39	1.19
5460	0.33203	1.58558	0.27002	4.22	1.14
10800	0.50890	1.31856	0.53704	2.13	1.14
12720	0.57165	1.16283	0.69277	1.81	1.25
18840	0.64146	2.87898	0.97662	1.22	1.19
25½ hrs.	0.71714	- Taken as T_∞ .			

Average $k_1 = 1.19 \pm 0.03 \times 10^{-4} \text{ sec.}^{-1}$

where k_1 is the rate of appearance of the corresponding ethyl ester.

$k_1/[\text{OAc}] = 2.49 \times 10^{-3} \text{ l/mole sec.}$

k_1 from plot $\approx 2.303 \times \text{slope} = 1.22 \times 10^{-4} \text{ sec.}^{-1}$

- TABLE XXV -

RUN # 87 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL 4-METHYLBENZENESULFINATE (XXXVIII) IN 100%

ETHANOL AT 90°C. WITH POTASSIUM ACETATE AS BASE. $[\text{Ester}] = 0.02465\text{M}$; $[\text{Acetate}] = 0.04776\text{M}$

$t_{\text{sec.}}$	$\text{Log } \frac{I_0-D}{I}$	$\text{Log}(D_\infty-D)$	$\text{Log} \frac{(D_\infty-D_0)}{(D_\infty-D)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^4 \text{ sec.}^{-1}$
0	----	1.87708	----	--	--
1200	0.13806	1.78919	0.08789	19.19	1.69
1800	0.18049	1.75816	0.11892	12.79	1.52
3000	0.29614	1.66026	0.21682	7.68	1.67
4200	0.36470	1.58973	0.28735	5.48	1.58
4800	0.39139	1.55884	0.31824	4.80	1.53
8400	0.55151	1.30533	0.57175	2.74	1.57
10200	0.62462	1.11018	0.76690	2.26	1.73
15780	0.68417	2.84092	1.03616	1.46	1.51
9½ hrs.	0.72144				
23 hrs.	0.75350	- Taken as T_∞ .			

Average $k_1 = 1.60 \pm 0.07 \times 10^{-4} \text{ sec.}^{-1}$

where k_1 is the rate of appearance of the corresponding ethyl ester.

$k_1 / [\text{OAc}^-] = 3.35 \times 10^{-3} \text{ l/mole sec.}$

k_1 from plot = $2.303 \times \text{slope} = 1.57 \times 10^{-4} \text{ sec.}^{-1}$

- TABLE XXVI -

RUN # 99 - THE SOLVOLYSIS OF p-METHOXYNEOPHYL 2-CHLOROBENZENESULFINATE (XXXIX) IN 100%

ETHANOL AT 90°C. WITH POTASSIUM ACETATE AS BASE. $[\text{Ester}] = 0.02492\text{M}$; $[\text{Acetate}] = 0.07960\text{M}$

$t_{\text{sec.}}$	$\text{Log } \frac{I_0 - D}{I}$	$\text{Log}(D_\infty - D)$	$\text{Log} \frac{(D_\infty - D_0)}{(D_\infty - D)}$	$\frac{2.303}{t} \times 10^4$	$k_1 \times 10^4 \text{ sec.}^{-1}$
0	0.03617	1.84346	---	---	---
360	0.19777	1.72897	0.11449	63.95	7.32
540	0.22848	1.70334	0.14012	42.63	5.96
720	0.29760	1.63942	0.20404	32.00	6.53
900	0.34418	1.59034	0.25312	25.58	6.48
1080	0.38741	1.53923	0.30423	21.31	6.47
1440	0.45614	1.44309	0.40037	15.99	6.40
1800	0.50263	1.36342	0.48004	-12.79	6.14
2220	0.59155	1.15226	0.69120	10.37	7.12
3 hrs.	0.73097				
5 hrs.	0.73353	- Taken as T_∞ .			

Average $k_1 = 6.55 \pm 0.33 \times 10^{-4} \text{ sec.}^{-1}$

where k_1 is the rate of appearance of the corresponding ethyl ester.

$k_1 / [\text{OAc}] = 8.23 \times 10^{-3} \text{ l/mole sec.}$

k_1 from plot = $2.303 \times \text{slope} = 6.67 \times 10^{-4} \text{ sec.}^{-1}$

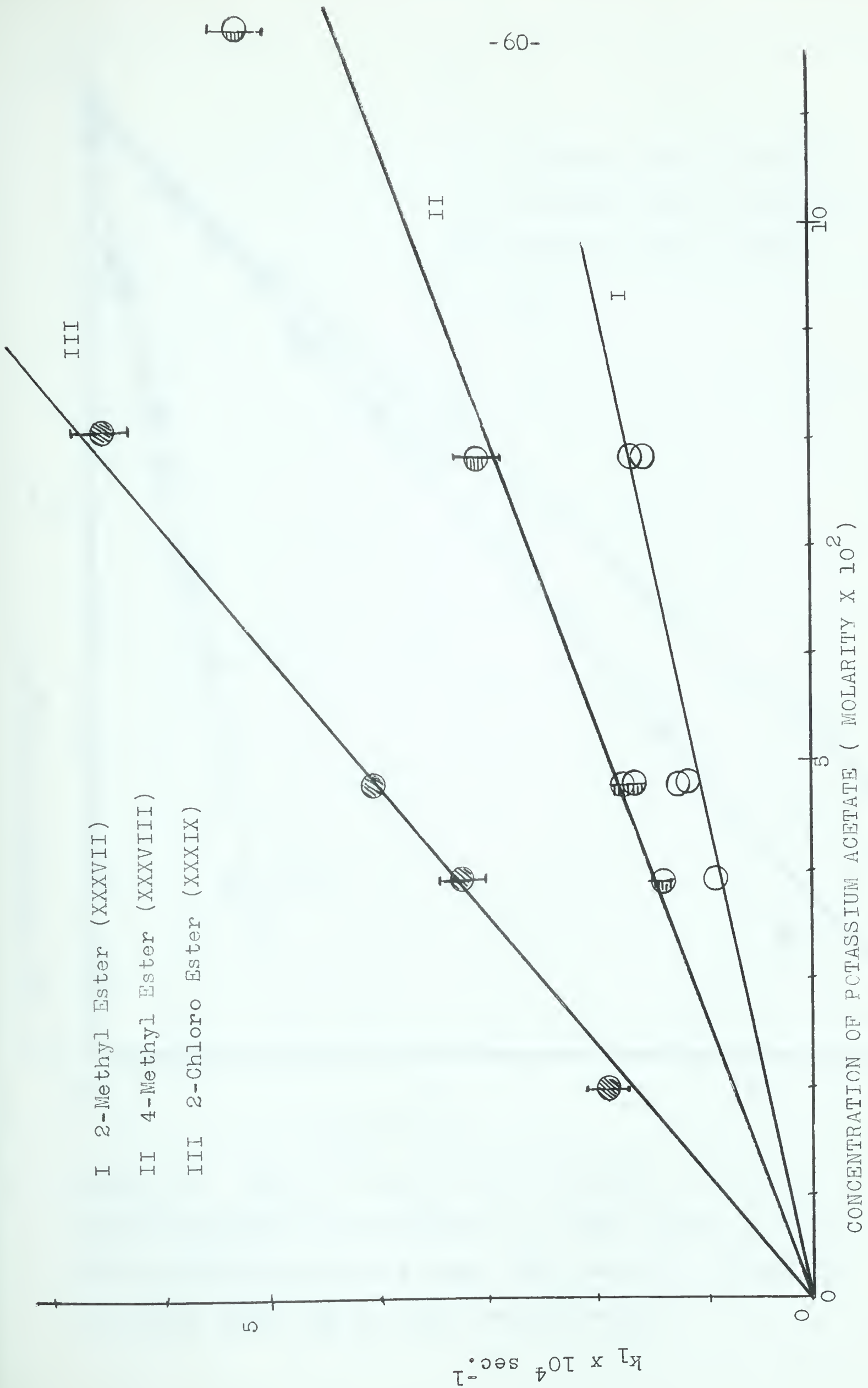


FIGURE 10: Plot of dependence of k_1 on concentration of potassium acetate in the solvolysis of various *p*-methoxyneophyl arylsulfonates in 100% ethanol at 90°C.

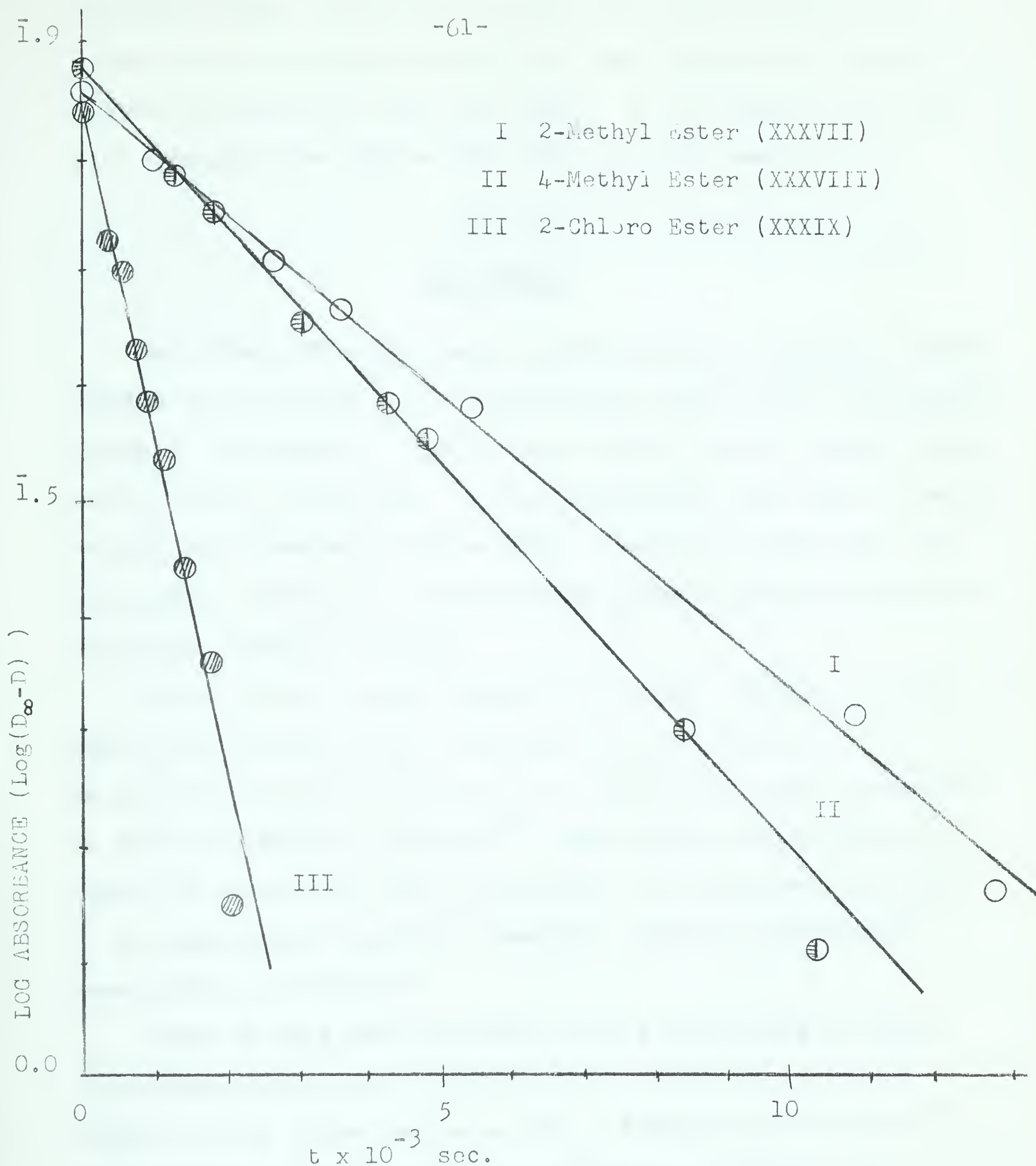


Figure 11: Plot of data for the solvolysis of various p-methoxyneophyl arylsulfonates in 100% ethanol at 90°C. with potassium acetate as base (see rates 92, 87 and 99 in Tables XXIV, XXV and XXVI respectively).

definite linear correlation in all three cases (Figure 10). A summary of the kinetic data from these experiments is presented in Tables XXI, XXII and XXIII, as are sample rates for each compound (see Tables XXIV, XXV and XXVI respectively).

Part IV

DISCUSSION

The effect of substituents in the sulfinato group on sulfur-oxygen bond cleavage may be examined by considering the relative rates of solvolysis of the various esters studied, under identical reaction conditions. Such a correlation has been attempted and is presented in Table XXVII. Relative rates have been calculated, taking the unsubstituted p-methoxyneophyl benzene-sulfinato (XXXVI) as unity.

In the column headed "Rates II", in Table XXVII, is data showing the effect of the variation in substituents on the second-order alkaline hydrolysis of substituted ethyl benzoates at 25°C. in "85%" aq. ethanol²⁷. This would seem to be a good model for comparison since hydrolysis, in both cases, proceeds by an acyl-oxygen type bond cleavage. Indeed, a reasonable correlation is observed.

Since no data were available on the solvolysis of ethyl 2,6-dimethylbenzoate in 85% ethanol at 25°C., an approximation to this value had to be made. Newman and co-workers⁴² had solvolysed methyl 2,6-dimethylbenzoate in 60% by vol. dioxane -40% water, at several temperatures ($k_2 = 1.50 \times 10^{-3}$ l/mole sec. at 125°C.). A plot of their data, with consequent extrapolation to 25°C. afforded $k_2 = 1.43 \times 10^{-7}$ l/mole sec. The relative rate of solvolysis of ethyl to methyl acetate under similar conditions⁴⁵ is 0.6, and the

- TABLE XXVII -

A COMPARISON OF THE RATES OF SOLVOLYSIS OF VARIOUS p-METHOXY-NEOPHYL ARYLSULFINATES AT 90°C. IN 100% ETHANOL WITH POTASSIUM ACETATE AS BASE.

Run	Ester	[Ester] M	[Acetate] M	$k_1^a \times 10^4 \text{ sec.}^{-1}$	Rel. Rates ^b		Lab. Book Ref.
					I	II	
98	2-Cl (XXXIX)	0.02486	0.04776	4.05 ± 0.25	1.45	2.24	89-2
85	4-CH ₃ (XXXVIII)	0.02465	"	1.60 ± 0.07	0.58	0.456	39-2
90	2-CH ₃ (XXXVII)	0.02510	"	1.15 ± 0.03	0.41	0.125	61-2
81	-H (XXXVI)	0.02502	"	2.78 ± 0.17	1.0	1.0	29-2
80	2,6-(CH ₃) ₂ (XXVII)	0.02422	"	0.0785	0.0282	0.0000121 ^c	173-2

a- Rate of formation of the corresponding ethyl ester.

b- Rates II refer to relative rates for the system

$\text{C}_6\text{H}_4\text{XCO}_2\text{Et}$, carried out in "85%" aq. ethanol at 25°C.

c- Value approximated from data on the solvolysis of

the corresponding methyl ester in 60% by vol. dioxane-water at 125°C.^{42,43,44.}

rates of saponification for substituted ethyl benzoates decrease by a factor of 11.4 on going from 60% dioxane to 85% ethanol^{43,44}. From these data, an approximate value for the rate of solvolysis of ethyl 2,6-dimethylbenzoate in 85% ethanol at 25°C. was calculated (7.52×10^{-9} l/mole sec.).

The decreased reactivity, with increasing substitution of methyl groups in the ortho position of the sulfinic group, can, presumably, be traced to a steric factor which becomes severe in the case of the 2,6-dimethyl compound. Here, back-side attack by acetate ion on sulfur is sufficiently hindered by the steric bulk of the two methyl groups which are in close proximity.

With the removal of the possibility of a steric effect by the substitution of a methyl group in the para position of the sulfinic group, the retardation observed may be ascribed to the electron donating properties of the methyl group alone.

The importance of this steric factor is again illustrated if one compares the rates of azide ion promoted sulfur-oxygen bond cleavage for p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) and p-methoxyneophyl benzenesulfinate (XXXVI), in 100% ethanol, in the presence of 2,6-lutidine. Removal of the two o-methyl substituents in the sulfinic group makes the sulfur atom about 30 times more susceptible to attack by azide ion.

The 2-chloro ester presents another view. Here, the electron withdrawing ability of the chlorine atom seems to be outweighing any steric factor, making the sulfur atom more electropositive, and consequently, more susceptible to attack by nucleophile.

PART V

EXPERIMENTAL

(i) Preparatory Work

All melting points were obtained on a Hershberg type melting point apparatus, using a set of Anschutz thermometers. All values stand uncorrected.

The infrared spectra were recorded on Perkin-Elmer Recording Infrared Spectrophotometers, Model P.E. 21 and Model 221G, using sodium chloride sealed cells. The Model P.E. 21 was utilized for kinetic measurements.

Refractive indices were obtained on a Bausch and Lomb Abbe-3L Refractometer, thermostated at 25°C. All values stand uncorrected.

The NMR spectra were recorded on a Varian Analytical Spectrophotometer, Model A-60.

The following standard procedure was adopted for chromatography of material on alumina. The column was prepared using thirty grams of Harshaw Alumina, Catalyst, Cat. No. AL-0109P, per one gram of substance to be chromatographed, dispersed in pentane. The compounds to be separated were then dissolved in the least possible amount of pentane or pentane containing a small amount of ether, and placed on the column. Various pentane-ether solutions were used for elution purposes.

PREPARATION OF p-METHOXYNEOPHYL ALCOHOL (XXXII) (see Chart I)

A. PREPARATION OF p-METHOXYBENZYL CYANIDE

This compound was prepared by the method of Rorig et al.²⁸ using molar quantities of anisyl alcohol. In the cyanation step, Mallinckrodt reagent grade acetone

was used as received without preliminary drying.

Found: %Yield: 60-75%; B.P. 115-116°C. (1.5 mm.);

$$n_D^{25} = 1.5277$$

Reported²⁸: %Yield: 74-81%; B.P. 94-97°C. (0.3 mm.);

$$n_D^{25} = 1.5285-1.5291$$

An infrared spectrum of the compound (CS_2) showed peaks at 2250 cm^{-1} ($-\text{CN}$) and 1250 cm^{-1} ($-\text{OCH}_3$). The NMR (CS_2) showed a singlet at 6.32 τ ($-\text{OCH}_3$) and a singlet at 6.50 τ ($-\text{CH}_2$) whose relative peak areas were 3:2.

B. α, α -DIMETHYL -p-METHOXYBENZYL CYANIDE

Sodamide was prepared from 33g. (1.43 moles) of clean sodium in one liter of liquid ammonia using a trace of ferric nitrate as catalyst²⁹. After the addition of 580 ml. toluene, the bulk of the ammonia was evaporated on a steam bath. p-Methoxybenzyl cyanide (86 g., 0.57 moles) was added and the last traces of ammonia were removed by heating at reflux temperature for 15 minutes.

Subsequent dropwise addition of 230g. (1.62 moles) methyl iodide, a 25% excess²⁵, to the reaction mixture was carried out as quickly as possible with gentle heating.

The resultant toluene mash was poured on ice and water, and the toluene layer separated and dried over anhydrous magnesium sulfate. Removal of the solvent at reduced pressure and consequent distillation of the brown oil residue afforded a clear colorless liquid, α, α -dimethyl -p-methoxybenzyl cyanide (B).

Found: %Yield: 50-60% ; B.P. 110-113°C.(2mm.);

$$n_D^{25} = 1.5142$$

Reported³⁰: %Yield: 53% ; B.P. 110°C.(3mm.)

$$n_D^{25} = 1.5143$$

Infrared spectrum (CS₂) showed absorption at 2232cm.⁻¹ (-CN) and 1250 cm.⁻¹ (-OCH₃). The NMR spectrum (CS₂) possessed a singlet at 6.28τ (-OCH₃) and a singlet at 8.41τ whose integration corresponded to a gem-dimethyl group. The relative peak areas were 3:6.

C. p-ANISYLDIMETHYLACETIC ACID

A 43 g. quantity of α,α-dimethyl-p-methoxybenzyl cyanide (B) was added to a solution of 45 g. potassium hydroxide in 150 ml. of 50% by vol. aqueous methanol. The mixture was heated for three days at reflux temperature.

After the reaction flask was cooled in ice, its contents were acidified with concentrated hydrochloric acid. The crude product separated as a brown oil which consequently solidified on prolonged cooling.

Clarification of a methanol solution of the crude acid with absorption charcoal (Norit), followed by two recrystallizations from aqueous methanol produced 29g. of shiny white plates (C).

Found: %Yield: 61% ; M.P. 88.0-89.5°C.

Reported²⁵: %Yield: 53% ; M.P. 88.0-89.5°C.

Infrared spectrum (CS₂) showed peaks at 1690 cm.⁻¹ (carbonyl), 1250 cm.⁻¹ (-OCH₃) and 940 cm.⁻¹ (-OH deformation). The NMR possessed a singlet at 6.32τ (-OCH₃), a singlet integrating for two methyls at 8.51τ, and

a singlet at -2τ ($-\text{OH}$). The relative peak areas were 3:6:1.

D. p-METHOXYNEOPHYL ALCOHOL (XXXII)

To a dispersion of 6g. (0.158 moles) lithium aluminum hydride in 200 ml. dry ether, 24g. (0.124 moles) of acid C in 150 ml. dry ether was added dropwise, over a period of one hour, at a sufficient rate to maintain gentle reflux of the ether. Reflux was continued for 24 hours with stirring.

At the end of this time, the aluminum complexes were decomposed by the dropwise addition of 12 ml. water followed by 10.8 ml. 10% sodium hydroxide solution to the reaction mixture. This treatment resulted in the formation of crystalline aluminum hydroxide, thus facilitating the isolation of product. The ether solution was washed once with water and dried over anhydrous magnesium sulfate. Removal of the ether by distillation afforded the crude alcohol, which, after two recrystallizations from petroleum ether (Skelley-B: B.P. 65°C.), gave large rhombic crystals of pure alcohol (XXXII).

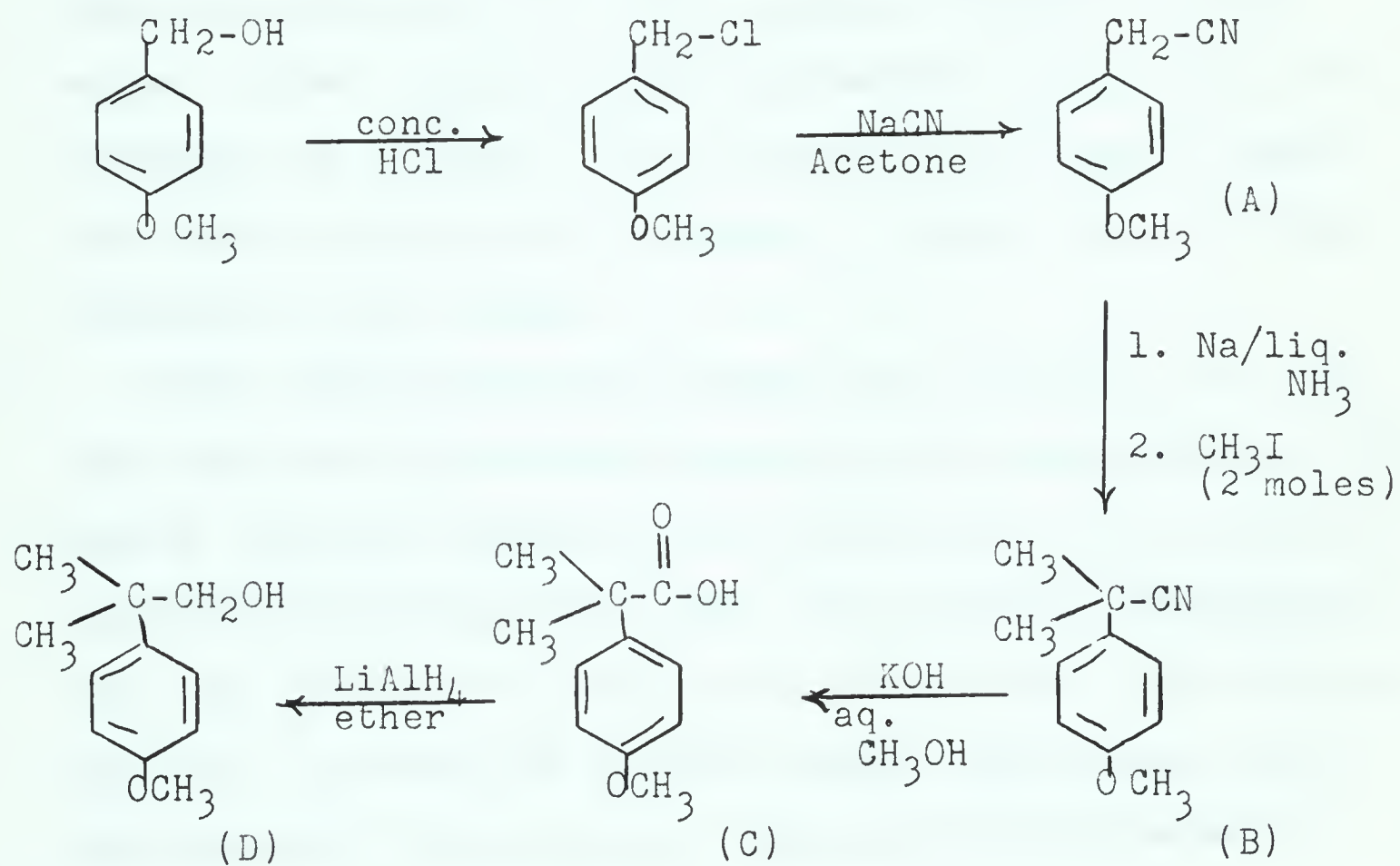
Found: %Yield: 90%; M.P. $46.5-48.5^{\circ}\text{C.}$

Reported²⁵: %Yield: 89.2%; M.P. $46.0-47.5^{\circ}\text{C.}$

Infrared spectrum (CS_2) showed absorption at 3590 cm.^{-1} ($-\text{OH}$), and 1250 cm.^{-1} ($-\text{OCH}_3$). The NMR spectrum (CS_2) possessed a singlet at 6.33τ ($-\text{OCH}_3$), a singlet at 6.68 ($-\text{CH}_2-$), a singlet at 7.78τ ($-\text{OH}$), and a singlet which integrated for a gem-dimethyl at 8.82τ . The relative peak areas were 3:2:1:6.

- CHART 1 -

THE PREPARATION OF p-METHOXYNEOPHYL ALCOHOL



THE PREPARATION OF BENZENESULFINIC ACIDS

The 2,6-dimethyl, 2-chloro, and 2-methylbenzenesulfinic acids were prepared by the method of Gattermann³¹, incorporating the modifications suggested by Hanke³². A sample preparation is given below.

2,6-Dimethylbenzenesulfinic acid (XXVI)

A cooled solution (5-10°C.) of 2,6-dimethylaniline (31 g.) in 250 ml. water and 27 ml. concentrated sulfuric acid was diazotized with 13 g. sodium nitrite in 40 ml. water. After sulfur dioxide was bubbled through the clear solution for 1½ hours, 125 g. electrolytic copper powder was added gradually with stirring. Cooling was continued throughout these steps.

When effervescence had ceased (in 1½-2 hrs.), the copper mash was filtered with suction, and extracted with 10% sodium carbonate solution. Acidification of the carbonate extract with 50% sulfuric acid, with cooling, precipitated the acid (XXVI) as an amorphous, white solid. The precipitate was filtered with suction, washed with 50 ml. water and air dried for one hour. The partially dry material was transferred to a vacuum desiccator and dried overnight, over phosphorus pentoxide, in vacuo.

Found: %Yield = 75% (32.6 g.) M.P. 95.0-98.0°C.

Infrared spectrum of the material (Nujol) showed absorption at 1090 cm.⁻¹, characteristic of S=O in sulfinic acids.

The unsubstituted and 4-methylbenzenesulfinic acids were prepared by Vogel's method³³, an example of which is given below.

Benzenesulfinic Acid

Steam was bubbled into 300 ml. water in a 3 liter

beaker until the temperature rose to 70°C. Zinc powder (40 g.) was added with stirring. To the mixture, 45.6 g. benzenesulfonyl chloride was added cautiously over a period of ten minutes such that the temperature of the mixture remained about 80°C. After raising the temperature of the slurry to 90°C. for ten minutes, 25 ml. 12M sodium hydroxide solution was added, followed by granular sodium carbonate until the solution was strongly basic. The mash was filtered with suction and the filtrate reserved.

The solid obtained was dispersed in 200 ml. water, and steam was bubbled through the mixture for ten minutes. Filtration of the mash afforded a second filtrate which, combined with the first, was evaporated on a hot plate in a stream of air, almost to dryness. Acidification of the residue with cold, dilute sulfuric acid gave benzenesulfinic acid. The solid was filtered with suction, washed with 50 ml. water, and dried in the manner described above for acid (XXVI).

Found: %Yield: 90.5% (33.5 g.) M.P. 84.0-86.0°C.

Reported³⁴: %Yield: 82.0% M.P. 85.0°C.

The sulfinic acids were invariably stored in a refrigerator to prevent decomposition. Their sodium salts, however, are quite stable at room temperature. Utilizing this fact, one can isolate the sodium salt in the second preparation and store the acid in this form until use.

- TABLE XXVIII -

A COMPARISON OF YIELDS AND MELTING POINTS FOR THE SUBSTITUTED BENZENESULFINIC ACIDS PREPARED.

Acid	M.P. °C.		Yield %		REFERENCE
	<u>Found</u>	<u>Reported</u>	<u>Found</u>	<u>Reported</u>	
2,6-(CH ₃) ₂ C ₆ H ₃ SOOH	95-98	---	70-85	---	---
2-CH ₃ C ₆ H ₄ SOOH	67-71	80	59.5	---	35
4-CH ₃ C ₆ H ₄ SOOH	82-83	85	91	90	33
C ₆ H ₅ SOOH	84-86	85	90.5	82	34
2-ClC ₆ H ₄ SOOH	111.0- 111.5	120	29.3	70	32

THE SULFINATE ESTERS

All the sulfinates were prepared by the same general method, a sample of which is given below.

p-METHOXYNEOPHYL 2,6-DIMETHYLBENZENESULFINATE (XXVII)

A mixture of 4.6 g. 2,6-dimethylbenzenesulfinic acid and 25 ml. pentane was treated with 15 ml. thionyl chloride in 15 ml. pentane. After vigorous reaction had subsided, the solution was quickly filtered through glass wool, and, after the bulk of the pentane and thionyl chloride had been removed at reduced pressure, residual traces of thionyl chloride were removed in vacuo by allowing the vessel to be evacuated for 3-4 hours. The residue, a brown oil, was dissolved in 15 ml. Karl Fischer grade pyridine stored over potassium hydroxide, and cooled to dry-ice-acetone temperatures.

To the cooled solution, a mixture of 5 g. p-methoxy-

neophyl alcohol (XXXII) in 25 ml. pyridine was added and the reaction was allowed to warm up to room temperature. The contents of the flask were poured over a mixture of ice and 35 ml. concentrated hydrochloric acid, slightly less than the equivalent amount which would be needed to neutralize the pyridine present.

The combined ether extracts from three extractions of the preceding mixture were washed thrice with water, with dilute hydrochloric acid until acid to litmus, twice with water, and with 10% sodium carbonate solution until no yellow color appeared in the aqueous layer. After the ether layer was dried over anhydrous magnesium sulfate, the solvent was removed by distillation on a steam bath to obtain a residual light brown oil, which was purified by elution chromatography.

Crystallization was induced by triturating the material at dry-ice-acetone temperatures, in the presence of a 10% ether in pentane solvent. The amorphous, white solid obtained was recrystallized from 10% ether-pentane to obtain 4.5 g. of a white solid, p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII), M.P. 57.0-58.5°C., in 50% yield.

Analyses, melting points and refractive indices for these esters are given in Table XXIX. A summary of the infrared and NMR spectral data on these compounds can be found in Table XXX.

All the sulfinate esters prepared were found to be unstable at room temperature if exposed to the air for an extended period of time. Consequently, these compounds were stored in the freezing compartment of a refrigerator before use.

DI-(2,6-DIMETHYLPHENYL)-THIOLSULFONATE

A 5 g. quantity of 2,6-dimethylbenzenesulfinic acid (XXVI) (0.029 moles) was dissolved in 75 ml. of water to which a trace of base (10 ml. 0.1M sodium hydroxide solution, 0.001 moles) had been added and the mixture was heated overnight on a steam bath.

The ether extract of the reaction mixture was washed with saturated sodium bicarbonate solution and dried over anhydrous magnesium sulfate. Removal of the solvent in vacuo yielded brownish, white crystals which on recrystallization from absolute ethanol gave 1 g. white solid (M.P. 121.5-124°C.).

%Yield: 36%

An infrared spectrum (CS_2) of the compound exhibited a sharp peak at 1325 cm^{-1} and 1145 cm^{-1} which have been assigned to thiolsulfonates³⁶.

p-METHOXYNEOPHYL p-TOLUENESULFONATE

The preparation was carried out in an analogous manner to that used for the sulfinic acid esters. From 4 g. p-methoxyneophyl alcohol and 7 g. p-toluenesulfonyl chloride, there was obtained a yellow, amorphous solid which, on recrystallization from petroleum ether-ether, yielded 4.3 g. white, amorphous solid of M.P. 44-46°C.

Reported²⁵: %Yield: 40-60% ; M.P. 44-46°C.

An infrared spectrum of the compound (CS_2) showed absorption at 1370 cm^{-1} and 1175 cm^{-1} , regions where p-toluenesulfonates are found to absorb³⁷, and a sharp peak was observed at 1250 cm^{-1} ($-\text{OCH}_3$).

- TABLE XXIX -

PROPERTIES AND ANALYSES OF SOME ARYLSULFINATES

ESTER	M.P. °C.	Refractive Index n_D^{25}	FORMULA	CARBON CALC. FOUND	ANALYSES % HYDROGEN CALC. FOUND	SULFUR CALC. FOUND
R = $-\text{CH}_2(\text{CH}_3)_2\text{CC}_6\text{H}_4\text{p}-\text{OCH}_3$						
2,6- $(\text{CH}_3)_2\text{C}_6\text{H}_3\text{SOOR}$	57.2-57.9	---	$\text{C}_{19}\text{H}_{24}\text{O}_3\text{S}$	68.84 69.08 68.85	7.28 7.31 7.18	9.65 9.81
2- $\text{CH}_3\text{C}_6\text{H}_4\text{SOOR}$	---	1.5638	$\text{C}_{18}\text{H}_{22}\text{O}_3\text{S}$	67.89 67.82 67.95	6.97 6.64 6.71	10.07 10.42
4- $\text{CH}_3\text{C}_6\text{H}_4\text{SOOR}$	51.2-52.0	---	$\text{C}_{18}\text{H}_{22}\text{O}_3\text{S}$	67.89 67.79 67.71	6.97 7.03 6.91	10.07 9.98
$\text{C}_6\text{H}_5\text{SOOR}$	---	1.5676	$\text{C}_{17}\text{H}_{20}\text{O}_3\text{S}$	67.07 67.31 67.14	6.62 6.55 6.81	10.54 10.40
2- $\text{ClC}_6\text{H}_4\text{SOOR}$	46.1-46.8	---	$\text{C}_{17}\text{H}_{19}\text{O}_3\text{SCl}$	60.27 60.40 60.29	5.61 5.52 5.56	9.46 9.34 9.47
2,6- $(\text{CH}_3)_2\text{C}_6\text{H}_3\text{SOOC}_2\text{H}_5$	47.3-48.6	---	$\text{C}_{10}\text{H}_{14}\text{O}_2\text{S}$	60.56 60.74 60.81	7.12 6.91 6.97	16.17 16.43
2- $\text{CH}_3\text{C}_6\text{H}_4\text{SOOC}_2\text{H}_5$	---	1.5338	$\text{C}_9\text{H}_{12}\text{O}_2\text{S}$	58.67 58.84 58.61	6.57 6.60 6.50	17.40 17.47
4- $\text{CH}_3\text{C}_6\text{H}_4\text{SOOC}_2\text{H}_5$	---	1.5307	$\text{C}_9\text{H}_{12}\text{O}_2\text{S}$	58.67 58.54 58.42	6.57 6.63 6.34	17.40 17.31
$\text{C}_6\text{H}_5\text{SOOC}_2\text{H}_5$	---	1.5317	$\text{C}_8\text{H}_{10}\text{O}_2\text{S}$	56.45 56.50 56.69	5.92 5.97 5.92	18.84 18.63
2- $\text{ClC}_6\text{H}_4\text{SOOC}_2\text{H}_5$ ^a	---	1.5486	$\text{C}_8\text{H}_9\text{O}_2\text{SCl}$	46.94 47.07 47.33	4.43 3.96 3.90	15.67 15.91

a- % Cl: Found = 17.24% ; Calc. = 17.32% .

A SUMMARY OF NMR AND INFRARED SPECTRAL DATA^a FOR SEVERAL ARYLSULFINATES^d

Ester	INFRARED IDENTIFYING ABSORPTION		Characteristic NMR Absorptions (τ) ^b				
			Ar-CH ₃	$\frac{-OCH_3}{-C(CH_3)_2}$	$\frac{-CH_2}{CH_3CH_2-}$		
2,6-(CH ₃) ₂ C ₆ H ₃ SOOR	1142 cm. ⁻¹	980 cm. ⁻¹	7.57(s)	6.34(s)	8.76(s)	6.16(s)	--
2-CH ₃ C ₆ H ₄ SOOR	1128 cm. ⁻¹	932 cm. ⁻¹ 952 cm.	7.78(s)	6.33(s)	8.78(s)	6.54(q)	--
4-CH ₃ C ₆ H ₄ SOOR	1130 cm. ⁻¹	935 cm. ⁻¹ 952 cm.	7.65(s)	6.33(s)	8.89(s)	6.52(q)	--
C ₆ H ₅ SOOR	1135 cm. ⁻¹	938 cm. ⁻¹ 952 cm.	--	6.34(s)	8.80(s)	6.48(q)	--
2-ClC ₆ H ₄ SOOR	1137 cm. ⁻¹	938 cm. ⁻¹ 957 cm.	--	6.34(s)	8.79(s)	6.42(q)	--
2,6-(CH ₃) ₂ C ₆ H ₃ SOOC ₂ H ₅	1132 cm. ⁻¹	882 cm. ⁻¹	7.47(s)	--	--	6.00(q)	8.72(t)
2-CH ₃ C ₆ H ₄ SOOC ₂ H ₅	1133 cm. ⁻¹	880 cm. ⁻¹	7.58(s)	--	--	6.32(m)	8.87(t)
4-CH ₃ C ₆ H ₄ SOOC ₂ H ₅	1135 cm. ⁻¹	880 cm. ⁻¹	7.59(s)	--	--	6.30(m)	8.83(t)
C ₆ H ₅ SOOC ₂ H ₅	1135 cm. ⁻¹	880 cm. ⁻¹	--	--	--	6.28(m)	8.83(t)
2-ClC ₆ H ₄ SOOC ₂ H ₅	1137 cm. ⁻¹	882 cm. ⁻¹	--	--	--	6.18(m)	8.78(t)
2,6-(CH ₃) ₂ C ₆ H ₃ SOOCH(CH ₃) ₂ ^c	1133 cm. ⁻¹	833 cm. ⁻¹	7.47(s)	--	--	$\frac{-CH-}{5.60(se)}$	

a- The solvent for all spectra was carbon disulfide.

b- Where s = singlet ; d = doublet ; t = triplet ; q = quartet ; se = septet ; m = multiplet

c- The gem-dimethyls were found to be non-equivalent.

d- Here, R = p-OCH₃C₆H₄C(CH₃)₂CH₂-

LITHIUM AZIDE

Neutralization of an aqueous solution of hydrazoic acid with purified lithium hydroxide to the phenolphthalein end point yielded this compound³⁸. The hydrazoic acid solution was prepared by the dropwise addition of 200 ml. 40% sulfuric acid solution into a boiling solution of 30 g. sodium azide in 300 ml. water. The 300 ml. distillate obtained was neutralized with a 50% solution of lithium hydroxide in water to the phenolphthalein end point.

The solution was evaporated almost to dryness on a steam bath, in a stream of air. The residue was again neutralized with a few ml. of hydrazoic acid solution and dissolved in ethanol. Removal of half the solvent by distillation followed by cooling of the residue, afforded crystallization of the salt. To obtain the anhydrous material, prolonged drying of the salt is required over phosphorus pentoxide, in vacuo.

(ii) SOLVENTS AND STOCK SOLUTIONS

PENTANE - Phillips Petroleum Company technical grade, n-pentane was distilled from phosphorus pentoxide before use.

ETHANOL - Absolute ethanol was prepared from commercial 95% ethanol by initial dehydration with calcium oxide, followed by treatment with magnesium ethoxide as described by Fieser³⁹. Karl Fischer titration of the solvent verified its anhydrous nature⁴⁰.

Aqueous ethanolic solutions were prepared by diluting this "100%" ethanol with distilled water, volumetrically, i.e., by the use of an automatic pipette, to obtain 40, 60, and 80% by volume solutions using the appropriate number of aliquots of ethanol and water, respectively.

STANDARD BASE - A sodium methoxide solution in methanol was prepared by the addition of a calculated amount of clean, bright sodium to one gallon of Fisher Certified anhydrous methanol. The resultant solution was standardized with N.B.S. standard potassium hydrogen phthalate. The solution, if tightly stoppered with a rubber stopper, can be used from 1-2 years without any appreciable change in titer.

STANDARD ACID - A solution of hydrochloric acid in distilled water was standardized with Fisher Certified anhydrous sodium carbonate, previously dried at 100°C. for one hour. Its titer was checked occasionally against the standard base.

STOCK SOLUTIONS OF 2,6-LUTIDINE - An accurately weighed out portion of 2,6-lutidine, previously distilled from potassium hydroxide, was added to a 100 ml. volumetric flask and diluted to volume with the appropriate solvent.

STOCK SOLUTIONS OF SALT IN ETHANOL - The salt was heated and dried at 78°C., in vacuo, to constant weight and quickly transferred to a flask containing 200 ml. absolute ethanol and fitted with a reflux condenser and drying tube. After a 2-3 hour reflux, the solution was concentrated to half its volume by distillation, and transferred quantitatively to a 250 ml. volumetric flask. Dilution to the mark was made with more absolute ethanol.

This procedure prevents the introduction of water, via the stock solutions, to reaction mixtures in "100%" ethanol.

The salts employed were:

Potassium Acetate - Fisher Certified Reagent.

Potassium Thiocyanate - B.D.H. Analar, recrystallized once from 95% ethanol.

Lithium Azide - As described in part (i) of this experimental.

(iii) KINETIC AND RATE MEASUREMENT PROCEDURE

A. LAMBERT-BEER LAW AND EXTRACTION PROCEDURE CALIBRATION

On certain of the p-methoxyneophyl arylsulfonates and on all of the ethyl arylsulfonates, a calibration of the extraction procedure and infrared measurement method used in following the rates of appearance or disappearance of the esters was carried out in order to determine if the compounds followed the Lambert-Beer correlation over the range of concentration employed.

An accurately weighed out portion of ester was dissolved in absolute ethanol in a 100 ml. volumetric flask such that the concentration of the resultant solution was about 0.025M, in ester, i.e., the concentration used in all rates. A five ml. aliquot of this solution was removed by means of a calibrated, automatic pipette and subjected to the extraction procedure described in section B. The residue from evaporation of the pentane extract served as the theoretical "100%" point.

Aliquots of standard ester solution were diluted volumetrically, with 100% ethanol by means of an automatic pipette such that the concentrations of the resultant solutions would be known fractions of the original standard solution. Again, a 5 ml. aliquot of each was withdrawn and subjected to the extraction procedure, to obtain residues whose compositions were known fractions of the 100% point residue.

All residues were diluted with two 1 ml. aliquots of carbon disulfide and the infrared spectra of these solutions

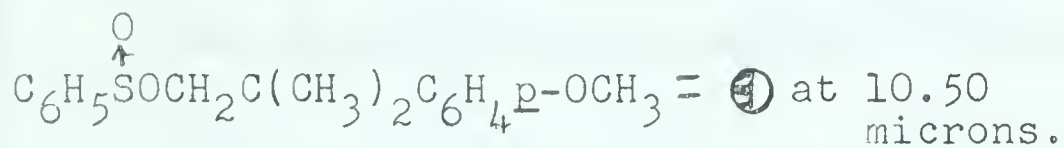
were determined on a Perkin Elmer Infrared Spectrophotometer Model 21, using the 20 cm. per micron scale, and scanning between 10.0-12.0 microns.

The corresponding $\log \frac{I_0}{I}$ values obtained from the spectra, were plotted against "% composition" to obtain the linear correlation. Plots of this correlation for the various compounds examined are presented in Figures 12-15.

- FIGURE 12 -

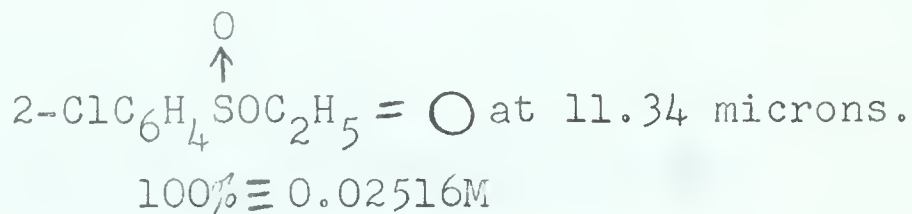
LAMBERT-BEER LAW AND EXTRACTION PROCEDURE CONTROL

PLOT OF ABSORBANCE vs. CONCENTRATION



(XXXVI) $100\% \equiv 0.02484\text{M}$

THEORETICAL % OF "100%" POINT (Concentration)



$100\% \equiv 0.02516\text{M}$

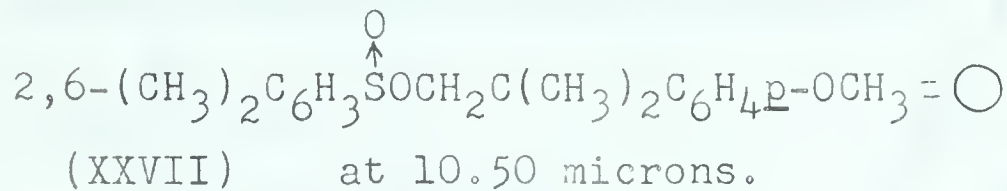
10 50 90

$\text{Log} \frac{I_0}{I} \times 10^2$ (Absorbance)

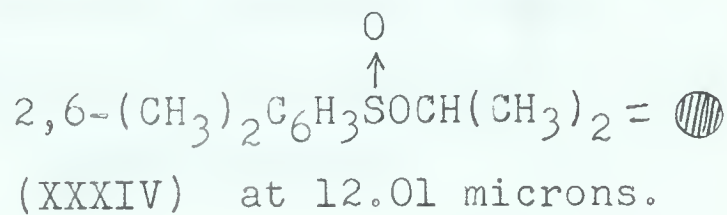
- FIGURE 13 -

LAMBERT-BEER LAW AND EXTRACTION PROCEDURE CONTROL

PLOT OF ABSORBANCE vs. CONCENTRATION



$100\% \equiv 0.02407\text{M}$



$100\% \equiv 0.02442\text{M}$

THEORETICAL % OF "100%" POINT (Concentration)

0

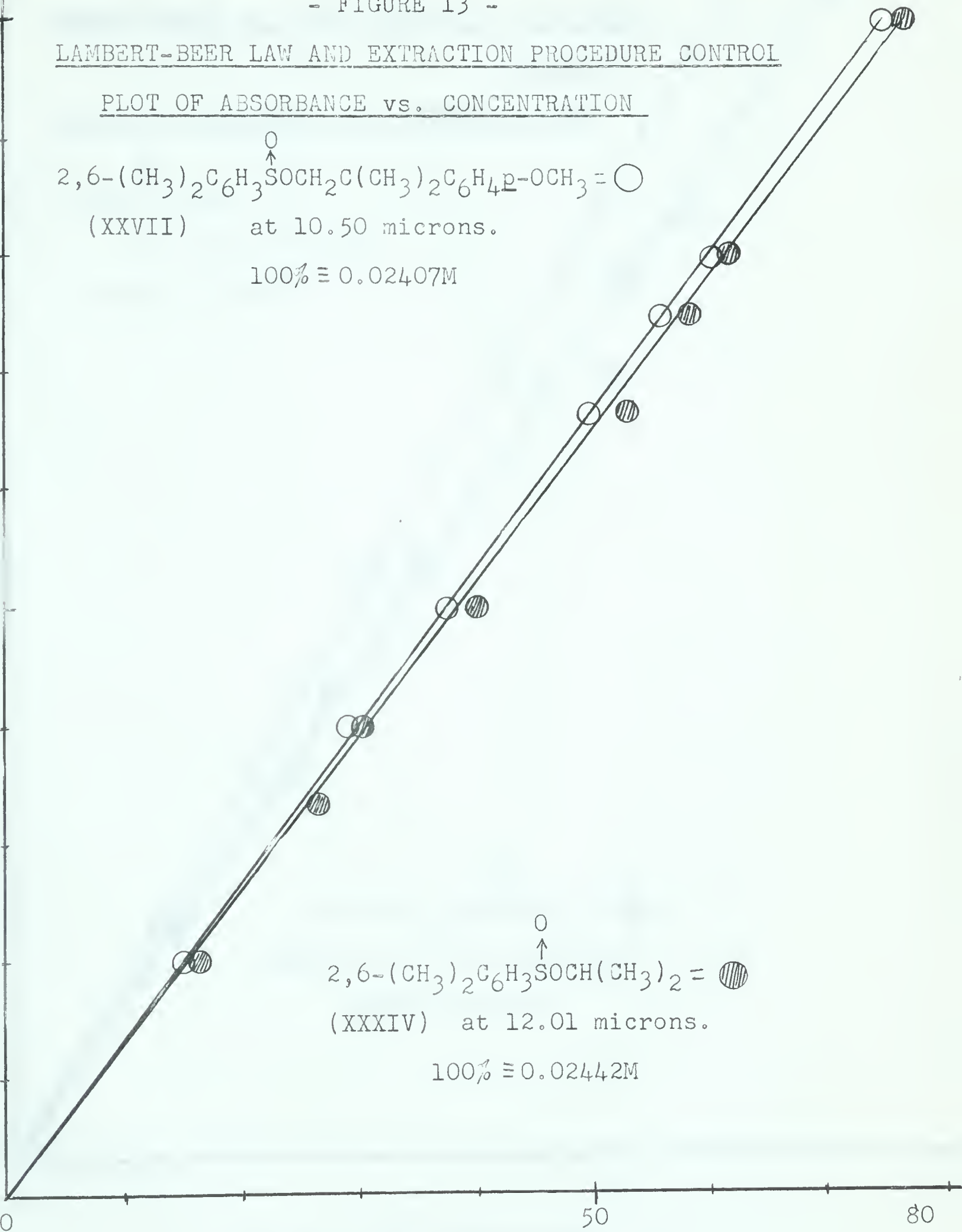
50

100

$\text{Log} \frac{I_0}{I} \times 10^2$ (Absorbance)

50

80

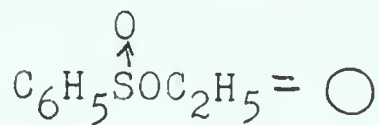


- FIGURE 14 -

LAMBERT-BEER LAW AND EXTRACTION PROCEDURE

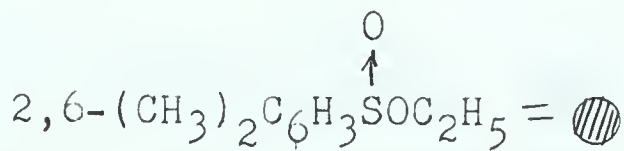
CONTROL

PLOT OF ABSORBANCE vs. CONCENTRATION



at 11.34 microns.

100% \equiv 0.02646M



•(XXXIII) at 11.34 microns.

100% \equiv 0.02453M

THEORETICAL % OF "100%" POINT (Concentration)

0

100

50

0

50

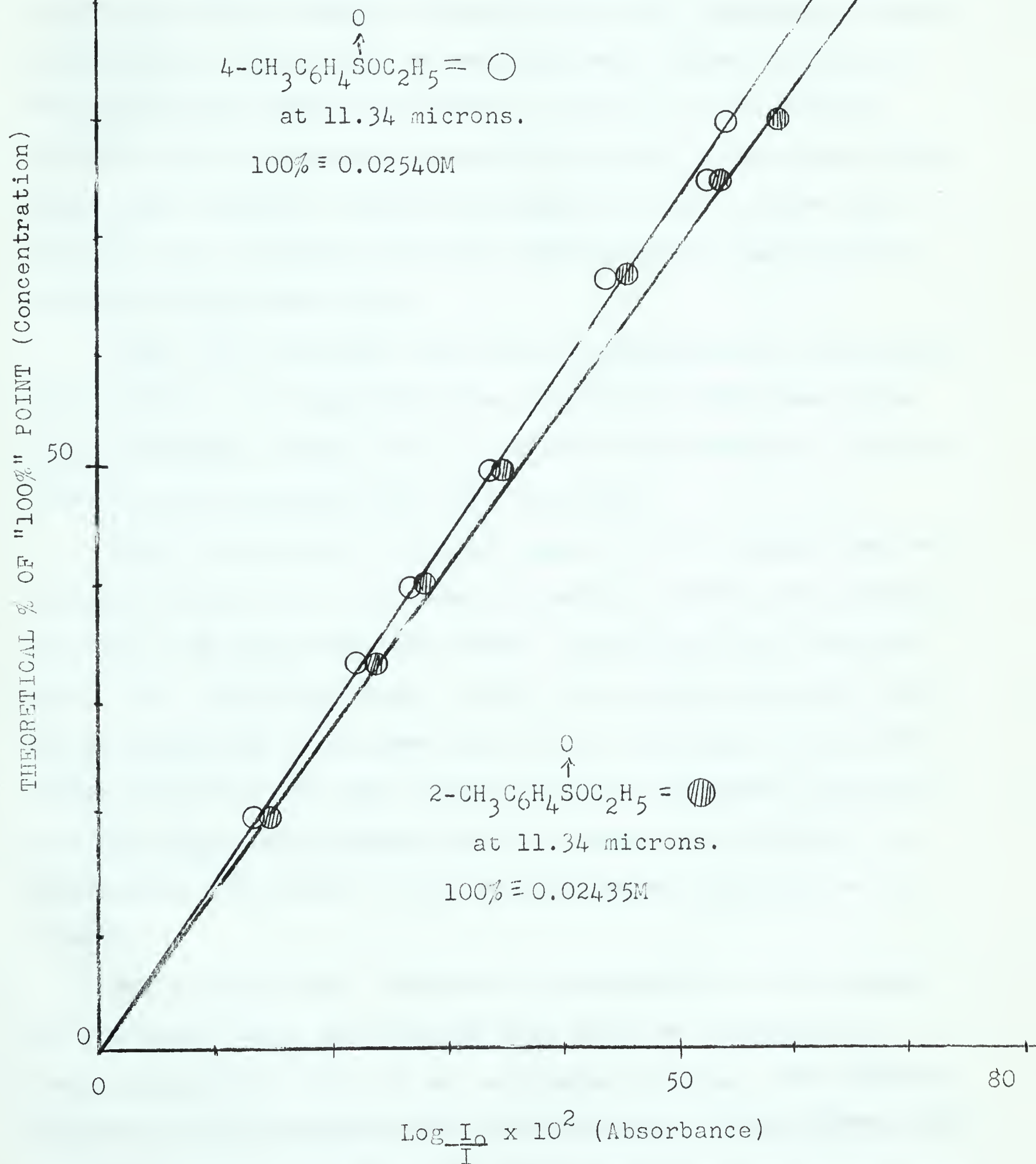
80

$\text{Log} \frac{I_0}{I} \times 10^2$ (Absorbance)

- FIGURE 15 -

LAMBERT-BEER LAW AND EXTRACTION PROCEDURE CONTROL

PLOT OF ABSORBANCE vs. CONCENTRATION



B. KINETIC MEASUREMENTS

An accurately weighed portion of ester was transferred to a 100 ml. volumetric flask. Enough solvent to dissolve the ester was added, together with as many 5 ml. aliquots of stock solution of base or salt as was required. After dilution to the mark with solvent and mixing, samples of the reaction solution were transferred to partially drawn out ampoules such that they contained slightly in excess of 5 ml. After the ampoules were sealed, they were immersed in the appropriate constant temperature bath.

After five minutes, one tube was withdrawn for the initial zero point. At appropriate time intervals, additional tubes were withdrawn, saving two for infinity measurements, and were quenched by thrusting them into ice water.

When the ampoule was broken open, a 5 ml. aliquot was removed by means of a calibrated automatic pipette, and delivered into a 60 ml. separating funnel containing 25 ml. pentane and 10 ml. distilled water. After the pentane layer was washed an additional four times with 10 ml. portions of distilled water, it was dried over sodium carbonate (anhydrous, granular) for one hour. The combined water washings were titrated for developing acid using a 0.1% phenolphthalein solution as indicator.

The residual oil, obtained by evaporation of the pentane at the water pump, was diluted with two 1 ml. aliquots of carbon disulfide with a 1 ml. automatic pipette. The infrared spectrum of this solution was determined on a Perkin Elmer Infrared Spectrophotometer Model 21 using the 20 cm. per micron scale and scanning from 10-12 microns. A reference cell of the variable spacer type was utilized so that any absorbance by the solvent

could be reduced to a minimum by compensation. This cell was also employed in section A for standardization purposes.

The preceding method applied only where the reaction was carried out above room temperature. In the case of those rates carried out at 25°C., a slight modification of this procedure was used.

After the reaction mixture of ester and base had been diluted to volume, and the solution had been properly mixed, the tightly stoppered 100 ml. volumetric flask was immersed in a constant temperature bath maintained at 25°C. After an equilibration period of five minutes, a five ml. aliquot of solution was removed by means of a calibrated automatic pipette and quenched by delivering it into a 60 ml. separating funnel containing 25 ml. pentane and 10 ml. water. At appropriate time intervals, additional aliquots were removed, saving two for infinity measurements. The remainder of the procedure was carried out as described above.

With the titrimetric rates, the aliquot of reaction solution was merely delivered into 25 ml. distilled water and titrated for developing acid using 10 drops of 0.1% phenolphthalein solution (in ethanol) as indicator.

C. PRODUCT RUNS

The procedure followed in product runs can be examined by considering a sample run given below(See run 37 on p.17).

An accurately weighed out portion of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) (0.925 g., 0.028M) was transferred to a 100 ml. volumetric flask. Aliquots of stock sodium ethoxide solution in 80% ethanol were added such that the resultant solution would be 0.041M in ethoxide ion. After the flask was diluted to the mark with more 80% ethanol, the mixed contents were transferred to a 250 ml. round bottom flask having a constricted neck. The flask was sealed and placed in a 90°C. constant temperature bath for a period of 25 hours.

After the ampoule had been removed from the bath and cooled in ice water, it was broken open and its contents were poured onto ice and enough hydrochloric acid was added to acidify the mixture (1 ml. 6M). The ether extract of this mixture was washed twice with water, twice with saturated sodium bicarbonate solution, once with water and was dried over anhydrous magnesium sulfate. Removal of the ether by distillation afforded a brown oil (0.753 g.).

At the same time, the water washings from above were acidified with concentrated hydrochloric acid, the solution saturated with sodium chloride, and the mixture was ether extracted twice. The ether extract was washed twice with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Removal of the ether in vacuo afforded a white solid which had an identical infrared spectrum and melting

point as 2,6-dimethylbenzenesulfonic acid (XXVI) (0.101 g., 21% yield).

The brown oil (0.753 g.) obtained previously was dissolved in 50 ml. pentane and placed on a column of Harshaw alumina (30 g.). Elution was consequently carried out taking 100 ml. fractions of the eluent for analysis as follows:

3 cuts	pentane	0.217 g.
1 cut	pentane-Skelley-B (50-50)	0.090 g.
1 cut	Skelley-B	0.033 g.
1 cut	CCl ₄ -Skelley-B (50-50)	---
1 cut	CCl ₄	0.097 g.
1 cut	80% CCl ₄ -20% ether	0.101 g.
1 cut	60% CCl ₄ -40% ether	0.019 g.

The weights refer to the residues obtained when the solvent was removed from these fractions.

Infrared spectra of these residues showed all but the first residue to be p-methoxyneophyl alcohol (XXXII), a total yield of 0.340 g. (68% yield). The first proved to be a mixture of p-methoxyneophyl 2,6-dimethylbenzenesulfinate (XXVII) and the corresponding ethyl ester (XXXIII). Comparison of the peaks at 10.42 microns ($\text{Log } \frac{I_0}{I} = 0.400$ for ester XXVII) and at 11.35 microns ($\text{Log } \frac{I_0}{I} = 0.170$ for ester XXXIII) showed these compounds to be in the ratio of approximately 2:1.

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